THE EPIDEMIOLOGY OF BLOOD COMPONENT TRANSFUSION IN EASTERN SCOTLAND IN 2000

Katherine J. Biggin

PhD (2007)
The University of Edinburgh

DECLARATION

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

(Katherine J. Biggin)

CONTENTS

LIST OF TABLES AND FIGURES

ACKNOWLEDGEMENTS

Foremost, I am indebted to the support and guidance of my supervisors Professor Robin Prescott and Dr. Pamela Warner (University of Edinburgh), and Dr. Brian McClelland (Scottish National Blood Transfusion Service), who I am also especially thankful to for creating this research opportunity and for providing the necessary clinical and transfusion medicine expertise.

Special gratitude goes to Amanda Stewart (Better Blood Transfusion Programme) for her enthusiasm, patience and friendship throughout the study but particularly in the early stages of study development and latter stages of thesis write up.

This study was supported and funded by the Scottish National Blood Transfusion Service for which I am especially grateful. I am thankful to the Effective Use of Blood group (Scottish National Blood Transfusion Service) for their continued interest, notably, Sandra Gray, Joyce Palmer and Yvonne Elliot. I am also especially appreciative of the involvement of Professor Tim Walsh (The Royal Infirmary of Edinburgh) and wish to thank him particularly for the opportunity to observe a liver transplant operation in which intra-operative cell salvage was used, during my first month on the study.

Specific acknowledgements for assistance with data sources and computing support go to Alan Sheriffs and Richard Dobbie (Information and Statistics Division, NHS(S)), Mike Murphy (National Blood Service) and Edward Stack (Scottish National Blood Transfusion Service). For assistance with developing literature searches I am indebted to June MacLeod (Scottish National Blood Transfusion Service) and Marshall Dozier (University of Edinburgh). For providing stimuli for additional research interests I thank Dr. Marc Turner (Scottish National Blood Transfusion Service), Stephen Dobra (Department of Health), Professor Sheila Bird (MRC Biostatistics Unit) and Dr. Alastair McGilchrist (The Royal Infirmary of Edinburgh).

The study was carried out in the Department of Public Health Science at The University of Edinburgh (2004-2007) and I wish to thank the staff and PhD peers for being encouraging and affable throughout.

ABSTRACT

BACKGROUND & AIMS

Blood transfusion is a globally accepted medical intervention that can save life and improve health but like many valuable therapies it also poses risk. From the patient perspective, therefore, it should therefore be prescribed only when it is absolutely appropriate to do so. Pressures on the blood supply also make it essential to promote the appropriate and effective use of allogeneic blood so as to preserve supply. The way blood is used within a given population needs to be carefully monitored and published evidence on blood use is available for various populations and settings. However, there is an increasing need for evidence about the patterns of use by clinical case group that can be used to identify areas where change in transfusion and clinical practice may be needed. The Scottish Transfusion Epidemiology Project (STEP) aimed to assess the feasibility of linking routine datasets of transfusion data and clinical data for blood use analysis. This thesis reports on the study of STEP data in order to describe blood component use by clinical case group and its application in exploring transfusion practice.

METHODS

This study employed computer-based methods to link the STEP data of transfusion day records (Scottish National Blood Transfusion Service) and Scottish Morbidity Record SMR01/cancer/death records (ISD Scotland). Clinically informed methods were devised to attribute blood component use to purposely defined clinical case groups. The study dataset was analysed to describe blood component use by age, gender and intensity of transfusion, and for surgical procedure and haematological disease clinical case groups. The impact of changes in transfusion practice and changes in population demographics on future blood use were modelled and further, additional applications were explored.

Results

The study dataset comprises information on blood component use for a subset of Scottish hospitals that received approximately 38% of the red blood cell units delivered by the Scottish National Blood Transfusion Service in the year 2000. The dataset contains 41,431 transfusion day records of blood component use that represent 21,309 transfused patients and the use of 60,130 red blood cell units, 4,795 platelet units, 9,446 fresh frozen plasma units, and 1,759 cryoprecipitate units. For red blood cell, platelet and plasma use, although a small proportion of patients were transfused intensively, they nevertheless accounted for a large proportion of blood component units.

17,403 (29%) red blood cell units were attributed to surgical events defined by red cell using procedures; 7,286 (12%) red blood cell units were attributed to 726 patients with a diagnosis of pre-malignant or malignant haematological disease. The remaining 59% of red blood cell units were not classified by clinical case groups in this study and represent areas for future work.

Between 2000 and 2031 the Scottish population is projected to remain fairly stable in size but to be proportionately older. Modelling the impact of this on the demand for blood indicates that by 2031 there will be a requirement for 38% more red blood cell units. The impact of applying best practice figures and potential savings using intra-operative cell salvage were modelled and identified potential savings in blood use.

Conclusion

The study linked available routine data and employed specific, novel methods to enable analysis of blood component transfusion, and specifically, blood component use by clinical case groups. The potential for employing the data in modelling analyses of blood component use and related applications was also demonstrated. Recommendations for future approaches to studying the clinical use of blood are made. The findings of the study can be used for future planning purposes and to inform guidelines and policy, with the aim of changing practice and promoting the appropriate use of blood.

DEFINITIONS AND ABBREVIATIONS

Table i. Definitions and abbreviations

Abbreviation	Terminology	Definition
A	**Assigned [blood component]**	A blood component unit that has been compatibility labelled for a patient and for which a blood bank transfusion record has been generated in the blood bank computer system.
ATICS	**Audit of Transfusion in Intensive Care in Scotland**	A prospective benchmarking study of transfusion practice in Scottish intensive care units.
BBTP	**Better Blood Transfusion Programme**	A Scottish Executive initiative which, in partnership with Donor Services Directorate and Blood Express Project, undertakes a range of initiatives that cover the transfusion process from donor to patient.
	Blood bank transfusion record	Record generated when a patients' blood sample was received for "Group and Save" (for blood grouping and detection of red cell antibodies, with sample saved for a maximum of 3 days in blood bank), or for the assignment of one or more blood component units to a patient.
BC	**Blood component**	Component of whole blood (Refer to Table 2.1 for details of individual components)
BDC	**Broad Diagnostic Category**	Clinical coding classification system for medical diagnostic information.
CABG	**Coronary Artery Bypass Graft**	A surgical procedure used to treat coronary artery disease using a blood vessel graft, usually from the leg, to bypass a narrowed or blocked coronary artery, thereby improving blood flow to the heart and reducing the chance of a heart attack.
CE	**Consultant episode**	The period of inpatient care under a specific consultant and/or in a particular ward between the dates of admission and discharge. The medical information pertaining to the consultant episode is written in the discharge letter and used in Standard Morbidity Records.
CIPS	**Continuous inpatient stay**	A specific pattern of inpatient stays defining the patient's profile that comprises one or more episode.

CRAG	**Clinical Resource and Audit Group**	Lead body within the Scottish Executive Health Department providing advice and promoting clinical effectiveness in Scotland. In 2003 CRAG became part of NHS Quality Improvement Scotland.
CRYO	**Cryoprecipitate**	A blood component prepared from fresh frozen plasma, which is rich in fibrinogen, factor VIII, von Willebrand factor, factor XIII, and fibronectin.
D	**Deassigned [blood component]**	A blood component unit that is no longer linked to a patient such as when blood is returned unused to the blood bank. The deassingnment is recorded in the blood bank transfusion record in which the initial assignment was recorded.
DRG	**Diagnosis-Related Groups**	Clinical coding classification system for medical information based on International Classification of Disease (ICD) diagnoses, procedures, age, sex, and the presence of complications or comorbidities.
EMAN	**East Manufacturing**	SNBTS blood component manufacturing site for Eastern Scotland.
EUB	**Effective Use of Blood**	A Scottish National Blood Transfusion Service research group. The main objective of the EUB group is to work with hospitals in Scotland in order to improve transfusion practice by means of a clinical effectiveness programme using audit, education and clinical research.
EUOBUP	**EU Optimal Blood Use Project**	A three year collaborative project to develop a pan-European standard for optimal blood use. Co-funded by the European Commission.
FFP	**Fresh frozen plasma**	A blood component prepared from plasma that is frozen within a specific period of time following collection.
g/dL	**grams per decilitre**	Unit of measurement of blood haemoglobin levels.
HDC	**Health Department Circular**	Memorandum issued by the Department of Health for England.
HIV	**Human Immunodeficiency Virus**	A retrovirus that can lead to Acquired Immunodeficiency Syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections.
ICD	**International Classification of Disease**	Clinical coding classification system for diagnostic information that defines the medical condition managed or investigated during an inpatient stay. These codes were used in the PhD study to define diagnostic case groups to which blood use could be attributed.

ICU	**Intensive Care Unit**	The branch of medicine concerned with the provision of life support or organ support systems in patients who are critically ill and require intensive monitoring.
IOCS	**Intra-operative cell salvage**	Medical procedure in which blood lost during surgery is recovered, and re-infused into the same patient following filter or wash cycles.
ISPOT	**International Study of Peri-operative Transfusion**	Research group investigating the use of new technologies to minimise peri-operative allogeneic blood transfusion.
ISD	**Information and Statistics Division**	Part of the NHS National Services Scotland, the national organisation for the management of health, information, statistics and information technology.
JPAC	**The Joint United Kingdom Blood Transfusion Services (UKBTS) and National Institute for Biological Standards and Control (NIBSC) Professional Advisory Committee**	The professional body in the United Kingdom for advising on, and publishing guidelines for, transfusion and tissue transplantation.
MEL	**Management Executive Letter**	Memorandum issued by the Scottish Executive Health Department (SEHD).
MHRA	**Medicines and Healthcare Products Regulatory Agency**	Government agency responsible for ensuring that medicines and medical devices work and are acceptably safe.
MSBOS	**Maximum Surgical Blood Order Schedule**	Guidelines for the maximum number of red blood cell units that can be cross-matched pre-operatively for a range of common elective, surgical procedures, based on and developed for specific, local clinical practices.
mths	**Month**	A calendar month.
NACO	**National AIDS Control Organisation**	Government agency in India responsible for control, surveillance, reporting and education issues relating to HIV/AIDS.
NHS(S)	**National Health Service (Scotland)**	The National Health Service in Scotland.
OPCS	**Office of Population Censuses and Surveys**	Clinical coding classification system for surgical operations and procedures that define the therapeutic or surgical intervention performed during the consultant episode. OPCS codes are arranged in pairs, where A details the main procedure code and B allows for the recording of supplementary codes for approach, technique, site or laterality. OPCS-4 codes were used in the PhD study to define surgical case groups to which blood use could be attributed.

PLT	**Platelets**	A blood component comprising blood cells that are responsible for blood coagulation and repair of damaged blood vessels.
RBC	**Red blood cells**	A blood component comprising blood cells that carry haemoglobin and help remove waste from tissues throughout the body.
SANGUIS	**Safe and Good Use of Blood in Surgery**	European-wide, multi-country, multi-centre study of blood component and product use in surgery.
SCCC	**Scottish Clinical Coding Centre**	Publishes guidelines and training manuals of clinical coding conventions for Scottish Morbidity Records for the Information and Statistics Division data schemes.
SD	**Standard deviation**	Statistical measure of variation.
SEHD	**Scottish Executive Health Department**	Health Department of the devolved Scottish parliament.
SHOT	**Serious Hazards of Transfusion**	Organisation which aims to build an evidence base of transfusion hazards and to promote national and international haemovigilance and to make recommendations for improvements in transfusion practice and patient safety.
SMR	**Standard Morbidity Record**	Record of hospital activity (consultant episode) generated from inpatient medical information recorded in discharge letters, and held by Information and Statistics Division (NHSS). Used in this study are SMR01 (Inpatients and day cases) and SMR06 (Cancer registration).
SMR01-CD	**SMR01/cancer/death record**	Linked SMR01/cancer(SMR06)/death(GRO) records used in this study
SNBTS	**Scottish National Blood Transfusion Service**	The specialist provider of transfusion medicine in Scotland that supplies blood, tissues, products and related services, and facilitates the safe and effective supply and use of blood.
SPSS	**SPSS**	Software package for statistical analyses (Versions 13.0 to 15.0 used in this study)
STED	**Scottish Transfusion Epidemiology Database**	The BBTP blood data management system that provides a population wide view of how transfusions are used in Scotland with the aim of identifying variation in practice, encouraging clinical review of blood use and contributing to the goal of reducing avoidable transfusions.
STEP	**Scottish Transfusion Epidemiology Project**	The Scottish National Blood Transfusion Service feasibility study that aimed to establish a link between SNBTS blood bank records and ISD SMR01/SMR06/GRO records in order to provide population based data on the use of blood components by NHS (Scotland) Trusts.

	Study period	The 1 year period from 1 January 2000 to 31 December 2000 inclusive, for which data was extracted for STEP (subsequently the study period of this study).
Tx	**Transfusion**	The process of transferring whole blood or blood components from a donor to a recipient by infusion.
yr	**Year**	A calendar year.
	Transfusion event	A general term for the use of blood due to transfusion.
TDR	**Transfusion day record**	The specific term for a blood bank transfusion record of units assigned extracted from the SNBTS Progesa blood bank computer system and compacted to comprise all transfusion events in a 24 hour period for one patient.
	Transfused patient/recipient	A patient with at least one transfusion day record in which the number of units assigned was more than the number deassigned.
U	**Used [blood component]**	A blood component unit deduced to have been infused into a patient. Calculated from units assigned minus units deassigned as recorded in a patient's blood bank transfusion record in a blood bank computer system.
vCJD	**variant Creutzfeldt-Jakob Disease**	An infectious agent of the group Transmissible Spongiform Encephalopathies (TSE), which causes a rare and fatal human neuro-degenerative condition and which can potentially be transmitted via blood transfusion.
UK	**United Kingdom**	
UKBTS	**United Kingdom Blood Transfusion Service**	A member group of JPAC
WMAN	**West Manufacturing**	SNBTS blood component manufacturing site for Western Scotland.
WHO	**World Health Organisation**	United Nations authority responsible for health by providing leadership and technical support, monitoring and assessing trends, and setting the research agenda and policy options for global health matters.
%	**Percentage**	

1. INTRODUCTION

1.1. INTRODUCTION

Transfusion medicine is under increasing pressures on a number of fronts. Blood is now safer from infection than ever before but the increasing requirement for safety measures makes blood an ever more expensive commodity. Serious hazards of transfusion such as incompatible transfusion and adverse reactions to allogeneic blood continue to pose a risk to transfusion recipients. Evidence for variant Creutzfeldt-Jakob disease (vCJD) transmission via blood transfusion is the latest concern to affect the use of blood and further, has impacted negatively on the supply of blood by limiting the potential donor pool. This and other pressures affecting donor eligibility and the availability of supply make more effective use of blood ever more necessary. Therefore, blood conservation strategies are being developed to reduce or replace allogeneic transfusions that, along with improved blood stock management and haemovigilance, are now essential considerations integral to transfusion practice to ensure the safe and appropriate use of blood. Another essential aspect of blood conservation is to monitor blood component use so that practice changes can be implemented in a targeted and evidence-based approach to ensure the effective use of blood.

Previous evidence focuses on audits or studies of blood use for populations that were restricted in time, setting or patient case mix. Few comprehensive, descriptive studies have been reported for the clinical use of blood for a whole population or well-defined, representative sample of a population for which an attempt was made to link transfusions to clinical information that represents the patient's underlying reason for transfusion. Reports that are available suggest that there is a decreasing trend in surgical blood use and a marked increase in blood use for medical conditions, to be anticipated particularly where there is an ageing population, but together they highlight methodological issues that represent areas requiring consideration and development by future studies.

The Scottish Transfusion Epidemiology Project (STEP) was a multi-centre, retrospective and epidemiological pilot study initiated by the Scottish National Blood Transfusion Service that was designed to assess the feasibility of data collection, linkage and analysis of routine datasets of transfusion and clinical data in order to inform the development of a continuous, automated blood use reporting system for the whole of Scotland.

The present study was an attempt to create a dataset and to devise methods to enable clinical blood use to be described for the Scottish population using routinely available and computerised sources of transfusion and clinical data. In this study the data that had previously been extracted for STEP was utilised. Data extraction and internal record linkage by patient identifier was performed by the Information and Statistics Division prior to the present study, but all subsequent data management, file restructuring and file merging processes formed part of this study. Relevant clinical methods were devised and epidemiological and statistical analysis of the data was performed. The computer software statistical package SPSS was used for data management and analyses.

1.2. STUDY SNYOPSIS

The aim of the study was two-fold. The first aim was to link available routine datasets of blood transfusion records and inpatient medical care records in order to construct a study dataset suitable for analysis. The second aim was to devise methods of analysis to describe the epidemiology of blood component transfusion in Scottish hospitals, specifically by clinical reason for transfusion, to help describe the population's need for blood.

In Chapter 2 a background to blood transfusion medicine, pressures on the supply of blood, and blood conservation strategies is provided. Chapter 3 provides a review of the range of published literature describing blood use, and in particular a review of comprehensive studies of blood use by clinical reason for transfusion as well as reflections on the methodology employed by previous studies.

Chapters 4 and 5 describe the materials, in particular the source data of blood transfusion records and inpatient medical care records, and the methods devised to link the source data in order to create a study dataset for subsequent analyses of blood component use.

In Chapter 6 the study dataset is described and in Chapter 7 the use of red blood cells, platelets, fresh frozen plasma and cryoprecipitate is reported, particularly for age distributions of blood component recipients and distributions of intensity of transfusion.

The use of red blood cells by purposely defined case groups for specific surgical procedures and for specific haematological conditions is reported in Chapters 8 and 9, respectively. Further, in Chapter 10 other questions about blood component use that can be explored using the study dataset are described, including analysis of donor exposure and, specifically, modelling the impact of the following factors on the use of blood:

- Changes in transfusion practice, for example the use of best practice indicators,
- The use of alternative interventions, for example intra-operative cell salvage,
- Changes in population demographics.

In Chapter 11 a discussion is presented that addresses the findings of the present study, in the context of previous reports, and of the strengths and weaknesses of the data and approach used. Furthermore, future areas of work are suggested and final conclusions are given.

2. BACKGROUND

2.1. BLOOD TRANSFUSION

The science of blood transfusion dates to the first decade of the 19th century though the first early attempts to transfuse animal blood were recorded as far back as the 15th century at a time blood was regarded as having mystical healing properties. The 19th century saw the discovery of distinct blood types, the first human-to-human transfusions, and the first use of blood transfusion to treat haemophilia (Thomas, 2005). The first reported use of transfusion in a military setting was the use of non-human albumin to replace lost circulating blood volume[1]. Since that time war has been a stimulus for developments in many aspects of blood collection, storage, transport and transfusion, as well as donor recruitment and blood services organisation. In the first half of the twentieth century the discovery of refrigeration and anticoagulants enabled blood to be stored and thereby facilitated routine, indirect transfusions in place of direct vein-to-vein transfusions. The discovery coincided with the First World War and led to the establishment of the first British Army blood depot. During the Spanish Civil War (1936-1939), a mobile field transfusion unit was set up, followed by a large-scale organisation of blood transfusion centres (Pinkerton, 2002; Coni, 2002). This development subsequently led to the establishment of the first blood banks such as in the Soviet Union where a system of national, large and subsidiary blood banks were set up. By World War Two an Army Blood Transfusion Service was set up in the UK to enable central recruitment of blood donors and efficient collection of blood, so as to increase the supply of blood to the military as it was required. By the end of the war more than half a million volunteer donors were registered and a donor service, much like the present day UK National Blood Services, was established. Within a few years the United States had followed suit (Thomas, 2005).

During the mid to late twentieth century a number of significant discoveries enabled notable advances in transfusion medicine. Whole blood was separated into red blood cells and

[1] Renwick, W. (1854) Transfusions in a case of cholera. *Dublin Medical Press.* **31**: 258-9 (Thomas, 2005)

plasma thereby improving the length of time blood could be stored for and meaning that separate blood components were available for use in different clinical situations (Table 2.1). The discovery of Rhesus antigens led to understanding of incompatibility transfusion reactions. Together, the production of plastic bags that replaced glass bottles and the development of new anticoagulant preservatives enabled safer and easier blood collection, storage and preparation. Fractionated blood products derived from the plasma component of blood were pioneered by Edwin Cohn (in 1940), opening up new treatments for a wide range of medical conditions, including diseases of the immune system, haemophilia and major blood loss reflected in medical practices today (Thomas, 2005).

Table 2.1 Blood components

Blood component	Description	Abnormalities
Red blood cells (Erythrocytes)	The most common cells in blood. Consist mainly of haemoglobin that carries oxygen from lungs to tissues of the body and carries waste product carbon dioxide away from tissues.	Low levels/abnormality causes anaemias, for example sickle cell, thalassemia; high levels/surplus causes erythrocytoses, for example polycythaemia vera.
White blood cells (Leukocytes)	Several different types with varying morphology and function. All help to defend the body against foreign materials and infectious disease by various immune processes.	Low levels predispose to infection in conditions such as leukaemia; high levels in some bone marrow disorders.
Platelets (Thrombocytes)	Activated by damage to blood vessels, adhere to the ruptured site and release various coagulation factors that are involved formation of blood clots.	Low levels predispose to bleeding in leukaemia and some immune disorders; high levels in some bone marrow disorders.
Plasma	The fluid in which other components are suspended: 92% water, 8% plasma proteins, and trace amounts of other components (e.g. hormones, antibodies, clotting factors). Cryoprecipitate is formed when normal blood plasma is cooled and is rich in Factor VIII.	Low levels of specific plasma proteins in haemophilia (Factor VIII deficiency causes bleeding), primary immune deficiency (Immunoglobulin deficiency predisposes to infections); high levels in bone marrow disorders, for example myeloma and macroglobulinaemia.

2.1.1. Blood conservation strategies

Blood transfusion is now globally accepted as a major medical intervention that can save life and improve health (WHO, 2004; McClelland, 2007). Donated blood is a precious gift: the collection and use of voluntary, non-remunerated blood donations is promoted by the World Health Organisation. The appropriate and effective use of the donor gift is paramount and the importance of blood transfusion today is undisputed but, as will be discussed in full in the following section (section 2.2), it is a practice that is placed under increasing pressures from many directions. Here, a range of approaches considered for reducing or replacing the need for allogeneic blood transfusion are discussed. The key elements are to conserve blood loss and to make safe and effective replacement where the need is considered to be absolute.

Better control of blood loss can be achieved by thorough pre-operative planning and patient management such as clinical assessments and blood testing; more difficult is rescheduling elective surgery for patients with specific contraindications for transfusion given the extensive planning issues relating to theatre and staffing logistics. However, during surgery, assessment of oxygen deprivation, monitoring of blood loss and judicious surgical and anaesthetic techniques can be used to reduce blood loss and make well-informed and appropriate decisions to transfuse. Post-operative monitoring and blood tests can be utilised to address post-operative bleeding and to provide detailed pathophysiological information about the patient which may negate the use or any further use of transfusion. These factors are concerned with conserving blood by improving patient management through careful monitoring and good clinical technique, related to which are other factors of organisational, educational and financial review (Provan, 1999; Lemos & Healy, 1996; Tinmouth *et al*, 2005; Madjdpour & Spahn, 2005).

The safe and effective replacement of blood implicates several techniques. Aside from autologous blood pre-donation and acute normovolaemic haemodilution (the replacement of donated autologous blood with volume expanders) that are not currently recommended for clinical practice in the UK (UKBTS, online), intra-operative and post-operative cell salvage are recommended ways of reinfusing a patient's own blood (washed or filtered) to effectively reduce or completely negate the need for allogeneic transfusion, particularly in cardiac and orthopaedic surgery (Carless *et al*, 2006). No safe blood substitutes have thus far

been developed (Lemos & Healy, 1996). Available transfusion alternatives are pharmacological agents including anti-fibrinolytics such as aprotinin and tranexamic acid, which promote blood clot formation, and recombinant erythropoietin, which stimulates red blood cell production (Madjdpour & Spahn, 2005; McClelland, 2007). Comprehensive evidence for the use of crystalloid and colloid plasma volume expanders is still needed and alternative oxygen carriers are still being developed. New and effective transfusion techniques and blood alternatives must be continually researched and assessed so that transfusion protocols and guidelines reflect the appropriate evidence base. Ultimately the balance of risk versus benefit must always be carefully considered prior to making the decision to transfuse.

2.2. PRESSURES AFFFECTING BLOOD TRANSFUSION MEDICINE

Increasingly blood transfusion is affected by a wide range of pressures and issues of controversy. This section describes these pressures that affect the supply of and the demand for blood as well as some general issues that have implications for the cost and resources associated with transfusion practice (Table 2.2).

Table 2.2 Summary of pressures affecting blood transfusion medicine

Diminishing supply (section 2.2.1-2)	Increasing demand (section 2.2.3)	Other pressures (section 2.2.4-5)
▪ New infection risks e.g. vCJD	▪ Ageing population	▪ Economics
▪ Additional tests for donated blood	▪ Changing epidemiology of diseases of the elderly	▪ Evidence-based guidelines
▪ Leucodepletion filtering	▪ Transfusion used in wider range of treatment programmes	▪ Clinical governance
▪ Population movements	▪ More complex/chronic disease	▪ New legislation and enforcement
▪ Difficulties recruiting and retaining young donors		▪ Public awareness

2.2.1. Supply: blood safety and risk reduction

While blood transfusion is safer now than ever before in countries with well developed health systems, it is not a practice without risk and current guidelines advise that it only be used when it is considered to be absolutely necessary, that is when the risk of not receiving blood outweighs the risk of transfusion (McClelland, 2007).

Since the 1970s a range of tests has been introduced to identify blood donations that are infected with transmissible viruses so that they can be removed from the supply chain and thereby reducing the potential risk of transmission of viral infection to the transfusion recipient. In the UK every donation must be tested for Human Immunodeficiency Virus (HIV, type 1 and 2), Hepatitis C (HCV), Hepatitis B (HBV), Human T-cell Lymphotropic virus I and II (HTLV-I and HTLV-II), and syphilis, and in America, due to differences in the epidemiology of infectious agents, West Nile virus and *Trypanosoma cruzi* (Chagas parasite)

are also tested for. Screening blood donations in this way has resulted in a substantial decrease in transfusion-transmitted infections and related deaths (Thomas, 2005).

Also posing a threat to blood recipients is bacterial contamination of blood components. This can cause immediate severe and sometimes fatal adverse reactions in the transfusion recipient. Contamination originates from an existing bloodstream infection in the donor or may occur at the time of blood collection from sources such as donor skin and collection equipment. Preventing transmission of bacterial infection relies on the use of sterile, single use equipment for blood collection and transfusion, screening at the point of donation by questioning the donor, and good collection techniques, including adequate skin preparation and the practice of diverting the initial blood flow to a separate collection pouch (Brecher & Hay, 2005). In some countries blood components, especially platelets, are cultured to detect bacteria before the blood is released for transfusion.

A majority of immediate adverse reactions related to transfusion are caused by blood group incompatibility (ABO incompatibility), that is the administration of blood of the wrong ABO blood group, such as giving donor group A, B or AB red blood cells to a group O patient. Medical errors of this type have serious consequences for the recipient, reportedly causing complications in one out of every 38,000 units of red blood cells transfused and causing twelve to thirteen deaths a year in the US (Dzik *et al*, 2003). Further, it is believed that transfusion errors, including ABO incompatibility as well as inappropriate transfusion and wrong dosing, are often underreported. Rates of wrong blood transfusion of between 16% and 30% have been reported in Australia (French *et al*, 2002).

The safety measures required to reduce the risk of administrative transfusion errors focus on the role of education of all staff involved in the process. The implementation of hospital transfusion committees and transfusion safety officers in some countries has begun to address the issue of education and has put patient safety first thereby improving the practice of blood administration (Dzik *et al*, 2003; Torella *et al*, 2002). However, even when blood is free of viral and bacterial contamination and is administered correctly, recipients are not free from transfusion-related risk of serious adverse reactions such as transfusion-related acute lung injury and transfusion-mediated immuno-modulation which can cause clinical complications, morbidity and even result in mortality (Goodnough *et al*, 1999).

Emergence of variant Creutzfeldt - Jakob disease (vCJD)

Currently in the UK, the greatest concern regarding blood transfusion safety is the emergence of the infectious agent variant Creutzfeldt-Jakob disease (vCJD). vCJD is a Transmissible Spongiform Encephalopathy (TSE) that was first described in March 1996 and is known to cause fatal neurodegeneration in humans. CJD was previously known to exist in three forms: sporadic (unknown cause), familial (genetic mutation), and iatrogenic (accidental transmission by surgery or transplant). This fourth, new form affects younger patients and has a longer illness phase. A link has been established between vCJD and exposure to Bovine Spongiform Encephalopathy (BSE), most likely through infected meat in the food chain. The link between vCJD and BSE is based on epidemiological, pathophysiologic and molecular features of the agents and resultant infection (WHO, online).

There is no evidence for the transmission of sporadic or familial CJD through the transfusion of blood or blood products but it is now accepted that the potential exists for vCJD to be transmitted by blood. To date there have been 165 confirmed and probable cases of vCJD in the United Kingdom (JPAC, 2007). Of the confirmed cases of vCJD, eighteen patients previously donated blood that was used by 66 recipients, of whom 24 are still alive. To date, four recipients of blood from donors who subsequently developed vCJD have been confirmed as being infected with the agent: one recipient was diagnosed with vCJD in 2003, one recipient died of unrelated causes in 2004 and two recipients have developed symptoms of clinical vCJD disease in recent years (2006 and 2007). It is likely that a proportion of people currently incubating the infection will never progress to clinical disease. Recent surveillance reports suggest that the trend in vCJD mortality has been falling since a peak in 2000 but the Joint United Kingdom Blood Transfusion Services (UKBTS) and National Institute for Biological Standards and Control (NIBSC) Professional Advisory Committee (JPAC) report of 2007 warns that further cases may arise due to secondary transmission via surgical instruments (JPAC, 2007).

The screening process that is currently available for vCJD is not completely reliable, potentially reporting false positives, and thus it is not routinely used. However, a recent announcement by researchers in Edinburgh suggests that a new test that currently identifies low levels of vCJD prion proteins in brain tissue could be developed further to test for prions

in blood and be introduced for routine use in testing donations by 2009. This announcement has prompted concerns about a loss of donors who do not wish to know if they are infected with vCJD. Professor Ian Franklin (National Medical and Scientific Director, SNBTS) has suggested that the number of donors could fall by as much as 20% even although it is expected that few people will actually test positive for vCJD (Moss, 2007).

In the meantime, current safety measures introduced so far in the UK include leucodepletion of all donated blood units, sourcing plasma for fractionation from outwith the UK, and withdrawal of blood components or tissues previously donated by individuals who are later diagnosed with vCJD. Further, exclusions prohibit whole blood and live bone donation by anyone who has received a blood transfusion in the UK since January 1980, and any donor whose blood was transfused to a recipient who later developed vCJD (JPAC, 2007). Other countries including America, Canada, Australia and France, have banned the donation of blood by people who have lived in the UK at any time since 1980 (WHO, online(b)).

Haemovigilance

Haemovigilance, the surveillance of serious adverse events (unintended occurrences associated with the transfusion process) and serious adverse reactions (unintended response of donor or recipient) that result in clinical complications, morbidity and mortality is now essential to improving transfusion practice. In 1996 the Serious Hazards of Transfusion (SHOT) reporting procedure was implemented in NHS and private hospitals in the UK and Ireland. The aim of the report is to collect data on actual and near-miss serious adverse events and reactions related to blood component transfusion in order to improve safety and standards, and to inform policy and guidelines for transfusion practice. Although voluntary, participation in SHOT is high and results indicate that the number of adverse events and near-misses related to blood transfusion has decreased since reporting began. Indeed, the risk of transfusion-transmitted infection has never been lower (Murphy, 2005). Further, since 2005 all blood banks and related establishments in the UK are required to notify adverse events and reactions to the Medicines and Healthcare products Regulatory Agency

(MHRA)[2] through a system called SABRE (Serious Adverse Blood Reactions & Events) (MHRA, online).

In the UK, in the seven years between 1996 and 2003, 23 million blood component units were supplied. The incidence of death from serious adverse reactions was 0.2 per 100,000 units of blood supplied and the incidence of serious morbidity from serious adverse reactions was 1.1 per 100,000 units of blood supplied. The risk of viral transmission per 100,000 units of blood supplied was estimated to be 0.014 for HIV, 0.024 for hepatitis C and 0.176 for hepatitis B. The figures indicate that the risk of transmission of viral infection via blood transfusion is low and major morbidity is more likely to be due to bacterial contamination. However, the risk of wrong blood transfusion was estimated to be slightly greater at 6 per 100,000, of which ABO incompatibility poses a risk of 1 per 100,000 (McClelland & Contreras, 2005a & 2005b). This data from the UK suggests that the overall risk of infection, morbidity and mortality from receiving blood transfusion is small. However, the risk does exist, particularly if a patient's lifetime exposure or recipients exposed to multiple transfusions for treatment of chronic conditions are considered. This issue reinforces the philosophy that transfusions should only be given when deemed clinically to be absolutely necessary.

2.2.2. Supply: influences on donor pool

An adequate blood supply that meets the needs of the population is essential. However, with changes to clinical and transfusion practice, developments in areas of new and alternative interventions and blood conservation strategies, and changes in demography and to the progression and patterns of disease, it is extremely challenging to define how much blood a population actually needs.

National blood transfusion services work constantly to ensure that adequate blood stocks are collected from healthy, adult volunteers. In countries with well-structured health care systems and blood transfusion services an adequate supply of blood is generally provided

[2] Medicines and Healthcare products Regulatory Agency (MHRA) is the UK government agency responsible for ensuring that medicines and medical devices work and are safe, and to whom serious adverse events or reactions related to the transfusion of blood and blood components should be reported.

and often taken for granted. However, in countries with disparate urban and rural health care provision or general poor health care provision across the whole country, a safe and reliable supply is more difficult to achieve (WHO, 2004; Goodnough *et al*, 1999; Enosolease, Imarengiaye & Awodu, 2004).

The donor pool is adversely affected by the increasing number of restrictions on donor criteria that are imposed in an attempt to increase the safety of blood (Cobain, 2004). To protect the donor, those with bleeding disorders, anaemia, diabetes mellitus and epilepsy are precluded from giving blood, and changes in the number of people with these conditions (and other conditions that may be implicated in the future) are likely to affect the number of potential donors (Donaldson, 2003). To protect the recipient from the risk of transmission of infection in donor blood, persons who have been exposed to malaria, HIV, hepatitis, syphilis and West Nile virus, as well as those who have had recent body piercing or tattoos, are requested not to give blood (SNBTS, online). The emergence of variant Creutzfeldt - Jakob disease (previously described in section 2.2.1) is the latest infectious agent to impact on the donor pool. The rise in the popularity and ease of international travel can promote the spread of infection by exposing a growing proportion of the world population to infections they wouldn't normally encounter. It is also becoming more difficult to engage the younger population in donating blood for reasons of travel and time constraints but also because of changing public awareness and attitudes to blood transfusion. Nevertheless, despite the impact on the donor supply, precautions are clearly essential for ensuring the greatest safety of donated blood product for the recipient as well as the safety of the donor.

Due to the pressures described, the recruitment and retention of donors is now a critical part of national blood services' programmes. It is particularly difficult for developing countries to maintain a stable and adequate donor pool. Repeat donors are reliable and are known to provide safe blood, thus conserving collection resources and reducing wastage (Thomson *et al*, 1998). It has been demonstrated that repeat donors who give blood for more than five years are less likely to test positive for viral infection than first time donors (Schreiber *et al*, 2001). In the UK and many other countries blood donors are volunteers and are not remunerated for their gift of blood. However, this is not the case in all countries. Where donors are paid there is concern about the reliability of responses to screening questions and hence about the safety and quality of donated blood (Donaldson, 2003).

2.2.3. Demand: demography and clinical epidemiology

The demand for blood is determined by a population's demography and medical needs, combined with clinical intervention and decision making processes that are influenced by healthcare provision, clinical practice and transfusion guidelines and strategies.

It is well documented in studies of blood use that a majority of transfusion recipients are elderly patients: for example, 53.3% (Vamvakas & Taswell, 1994) and 57.0% (Mathoulin-Pelissier *et al*, 2000) of red blood cells were reported to be transfused to patients aged over 65 years. The elderly suffer a higher incidence of concurrent medical conditions than younger people and are less likely to be able to tolerate being anaemic, hence their greater requirement for blood transfusion (Wells, 2004). With population expansion expected in the older age groups over future years the resulting increase in the demand for blood will put pressure on the supply chain.

Along with a change in population demographics, a change in clinical disease trends and treatments will also affect the demand for blood. Transfusion was traditionally used to counter blood loss due to surgery, trauma and obstetric complications but there is an increasing requirement for blood as a supporting intervention in the treatment of a whole range of clinical conditions as advances in medicine, for example cancer treatments, and surgery, for example organ transplant, are made (Pitocco & Sexton, 2005). In conditions such as leukaemia effective treatment with chemotherapy, irradiation, and transplantation of bone marrow can only be effectively undertaken if transfusion of red blood cells and platelets is available to support the patient during periods of bone marrow suppression.

Improved survival rates, increased rates of comorbidity and complex or chronic disease, wider use of transfusion in the treatment of medical conditions and the ageing population all contribute to an increased demand on the blood supply.

2.2.4. Resource and regulatory pressures

The economic cost of blood reflects the cost of collection, processing and testing of blood components as well as the supply of blood to the end-user, the transfusion recipient. Costs associated with the testing and production of blood suitable for transfusion are escalating as new measures are introduced to improve the safety and quality of blood. Extensive developments include viral infection testing, and testing to detect abnormal prion protein in donated blood in tandem with prion removal filtration. Specifically, in the UK since 1995, the cost of blood has risen substantially because of the measures introduced to reduce the risk of vCJD transmission through blood transfusion (Lin, 2004). Prion removal filtration of blood components to reduce the risk of Transmissible Spongiform Encephalopathy infectivity such as vCJD is likely to add an estimated £100 million to the cost of blood provision by the NHS (Murphy, 2005; Burnouf & Padilla, 2006). Costs associated with implementing measures to improve safety and efficiency of hospital blood transfusion practices such as hospital transfusion committees and transfusion safety officers, research initiatives and reporting systems add to the total cost of providing a transfusion.

The infrastructure of blood services vary by country and depending on need. In Denmark blood collection is decentralised and based in hospitals. In the USA several large organisations, including the American Red Cross, Americas Blood Centres, compete for blood collection activities. Some countries, for example Hong Kong, have found that outsourcing aspects such as product delivery saves money and frees up resources in other areas of the blood service and supply chain. Economic and resource constraints on the infrastructure of blood services have prompted some developed countries, including the UK, France, Canada and Australia to centralise their services thus enabling them to reduce the number of testing and production sites whilst increasing levels of accountability and quality. Developing countries however can find it difficult to centralise services due to a lack of resources and investment; it should be regarded as the responsibility of international organisations to help them to establish suitable infrastructures that can deliver appropriate and sustainable services (Lin, 2004).

It is a complex issue for the blood services to deliver a sustainable service not least because it is difficult to predict the influence of factors such as large scale infection outbreaks (for example Severe Acute Respiratory Syndrome (SARS) in 2002/3, or a winter influenza epidemic), emergency incidents including terrorist attacks, natural disasters and seasonal variations (Lin, 2004; Donaldson, 2003). As part of stock management, hospitals should make contingency plans to deal with potential blood shortages.

The variations in temporal and logistical factors related to providing an adequate blood supply means shortages can not always be predicted although advances are being made in automated, time-series forecasting programmes (Pareira, 2004). Well-developed blood transfusion services use production planning models to try to predict demand in order to keep adequate supplies whilst minimising wastage (Lin, 2004). The UK Blood Stock Management System is a database of blood unit issues, stock inventory, wastage and shelf life operated as a partnership between the National Blood Service of England and North Wales and hospitals with participation on a voluntary basis. The Blood Stock Management System enables analysis of the entire supply chain, provides real-time monitoring of stock management, is used for benchmarking of transfusion practices, and can be used to drive improvements such as reducing inventory levels (Chapman & Hick, 2003; Donaldson, 2003). In America, National Blood Data Resource Centre (NBDRC) surveys of the blood supply highlighted concerns that according to projected trends up to the year 2000, demand would start outstripping supply and so a government sponsored programme to monitor supply and predict shortages was implemented (Nightingale *et al*, 2003). With this sort of resource available, stock management systems can have practical and beneficial impact on the blood supply thus helping to reduce the effect of growing pressures. However, more information is needed on the clinical use of blood and patient outcome following transfusion in order to better inform such models of supply and demand.

For transfusion practice, resource requirements go beyond the practical issues of finance and infrastructure. In addition, blood transfusion practice relies on social factors such as local clinical practice, public understanding and expectations of clinical treatment and blood transfusion, as well as a knowledgeable donor community to provide an adequate and sustainable blood service (Lin, 2004).

Further, resource provision and utilisation is increasingly influenced by regulatory pressures. Legislation increasingly enforces standards on prescribing, ordering, collecting, storing and administering practices involved in the provision of blood components for transfusion such as the 2005 UK Blood Safety and Quality Regulations (Cobain, 2004). However, comprehensive evidence-based guidelines on the appropriate use of blood for all clinical contexts are not available. The Handbook of Transfusion Medicine sums up the concern:

> "Correctly used, blood and blood products can save lives and provide clinical benefit to many patients. However, aspects of blood transfusion practice have not been rigorously proved by clinical trials so it is impossible to give a completely evidence-based account." (McClelland, 2007)

It is generally accepted that transfusion practice should be based on national guidelines that are informed by evidence-based medicine but where evidence is lacking, compliance with guidelines and appropriateness of transfusion can be hard to measure (Wallis, Stainsby & McClelland, 2002). Where appropriately conducted, audits and monitoring programmes can be used to identify areas for practice intervention and assess the effect of change on transfusion practice in the hope of improving the appropriate use of blood (Kanter, 1998; Goodnough *et al*, 1999). A full review of studies relating to transfusion medicine practise is reported in Chapter 3. The policy responses of the United Kingdom that aim to improve the safe and effective use of blood are considered next (section 2.3).

2.3. UK POLICY AND SCOTLAND SPECIFIC RESEARCH IN RESPONSE TO IMPROVING BLOOD TRANSFUSION MEDICINE

In this section an overview of the policy response of the United Kingdom with respect to transfusion medicine is presented. The actions required to improve the safety and efficacy of blood use are described in a series of Health Department Circulars (HDC) (England) and Management Executive Letters (MEL) (Scotland). The recommendations provide the context in which developments in monitoring and analysis of the use of blood components in transfusion, such as the present study, were prompted.

In the summer of 1998 the UK Chief Medical Officers held a symposium entitled "Evidence-based blood transfusion" that focused on improving transfusion practice throughout the National Health Service (NHS). It brought together a range of transfusion specialists, clinicians and managers from NHS trusts to discuss requirements to ensure the safe and effective use of blood in light of increasing demands for use, decreasing donations, rising costs, emerging risks associated with vCJD, implications of clinical governance, SHOT reporting, the waiting list initiative and changing perceptions of clinicians and the public.

The symposium focused on variations in blood use, the evidence base for best practice and the need for monitoring to improve understanding of patterns of blood use. It concluded that improvements could be made by all stakeholders to ensure safe, effective and appropriate use of blood for the future. The recommendations formed the "Better Blood Transfusion" Health Service Circular, HSC 1998/224 (Department of Health, England, 1998) and Management Executive Letter, MEL (1999)9 (Scottish Executive Health Department (SEHD), 1999a). The minimum recommendations are summarised in Table 2.3a. Further recommendations considered to need additional consultation at that time are given in Table 2.3b.

A follow-up symposium held in 2001 was jointly organised by the National Audit Office, the National Blood Service and the Department of Health, and was attended by the UK Chief Medical Officers. It was agreed by those in attendance that progress had been made since 1998 with the formation of Hospital Transfusion Committees and satisfactory engagement in the SHOT reporting system. The 2001 symposium focused on further promoting integrated

and collaborative approaches to improving transfusion practice. The recommendations and updated action plan were published in Health Service Circular, HSC 2002/009, "Better Blood Transfusion – Appropriate use of blood" (Department of Health, England, 2002) and NHS HDL (2003)19 (SEHD, 2003).

Table 2.3a Minimum recommendations of HSC 1998/224 to be implemented in all NHS Trusts where blood is transfused

Time scale	Action
From March 1999	▪ Ensure Hospital Transfusion Committees in place to oversee all aspects of transfusion.
	▪ Participate in annual SHOT enquiry.
By March 2000	▪ Agree and disseminate local transfusion protocols based on guidelines and best practice.
	▪ Support local transfusion protocols with training.
	▪ Explore feasibility of autologous blood transfusion and ensure patients aware of option where appropriate.
	▪ Consider introduction of peri-operative cell salvage

Table 2.3b HSC 1998/224 recommendations requiring further discussion

Action
▪ Extend accreditation of haematology laboratories to include whole of transfusion service (i.e. including hospitals).
▪ Integrate national advice systems for blood and tissue safety and consider the development of a web site for the exchange of good practice.
▪ Carry out systematic review and research into clinical and cost effectiveness of blood component therapy and variations in transfusion practice.
▪ Consider potential role of a specific Blood Transfusion Medicine academic department.
▪ Consider potential application of new technologies to improve transfusion.
▪ Carry out comparative audit in blood transfusion practice.
▪ Review the regional and national organisational structure of blood user groups and patient representation.

The themes laid out in the recommendations are the foci of a range of projects in the United Kingdom. The significant projects and studies carried out in Scotland over more than a decade share the common aims of increasing understanding of how and why blood is transfused and striving to optimise the use of blood, setting the context in which the STEP feasibility study was initiated (Table 2.4). The projects represent collaborative efforts that have made, and are continuing to make, advances in promoting the safe and effective use of blood.

Table 2.4 Blood use projects in Scotland (1991 to present day)

Project title	Aim
Participation in SANGUIS project (Data collected 1991, Published 1994)	European-wide, multi-country, multi-centre study of blood component and product use in surgery.
Optimal Use of Donor Blood Report (1995)	Clinical effectiveness project funded by Clinical Resources and Audit Group (CRAG), Scottish Executive Health Department (SEHD).
Formation of SNBTS Effective Use of Blood group (1999)	An SNBTS research group whose main objective is to work with hospitals in Scotland in order to improve transfusion practice by means of a clinical effectiveness programme using audit, education and clinical research. Project Manager: Sandra Gray (SNBTS)
Participation in International Study of Peri-operative Transfusion (ISPOT) (1999-2004)	Research group investigating the use of new technologies to minimise peri-operative (elective surgery), allogeneic blood transfusion.
Scottish Transfusion Epidemiology Project (STEP) (2000)	SNBTS pilot project to assess the feasibility of collecting and linking routine transfusion and clinical data for use in analysis of clinical use of blood. Current PhD study developed from this.
Safe and Effective Transfusion in Scottish Hospitals study (2000-2003)	CRAG/SEHD funded study investigating the role of the Nurse Transfusion Specialist, in clinical quality assurance and improvement following MEL 1999(9) "Better Blood Transfusion". Project lead: Sandra Gray (SNBTS)
Better Blood Transfusion Programme (BBTP) (2004)	In partnership with Donor Services Directorate and Blood Express Project, undertakes a range of initiatives that cover the transfusion process from donor to patient.
Scottish Epidemiological Database (STED) (2005)	The BBTP blood data management system that provides a population wide view of how and why transfusions are used in Scotland with the aim of identifying variation in practice, encouraging clinical review of blood use and contributing to the goal of reducing avoidable transfusions.
EU Optimal Blood Use Project (EUOBUP) (2007)	A three year collaborative project to develop a pan-European standard for optimal blood use. Co-funded by the European Commission.

3. LITERATURE REVIEW

3.1. INTRODUCTION

Current pressures affecting transfusion practise include the risk posed by the emergence of vCJD, rising costs associated with blood safety initiatives and regulatory requirements, public perceptions of risk, the ageing population and a change in the epidemiology and treatment of disease (section 2.2). In this changing environment patterns of blood use must be monitored in order to provide information for the way blood is used by a given population. The information can be subsequently used to inform guidelines, policy and strategies that promote practice change in order to achieve appropriate transfusion in all settings and to relieve the practice of the pressures it is under.

Audits and descriptive analyses of blood component use for specific groups of patients, typically those that are relatively straightforward to categorise, such as patients undergoing major surgical operations, are frequently reported. However, rather fewer studies report on the use of all blood component types across the full spectrum of patients who have conditions, or who undergo treatments, that may require transfusion. The evidence that does exist highlights the range of difficulties with this type of research.

Examples of audits, outcome studies and descriptive studies that have contributed to informing the evidence base about the use of blood for transfusion are described here (sections 3.2-3.4). Finally a review of quantitative descriptive studies of red blood cell use related to clinical case group is reported and the methodological factors that must be addressed to allow for useful research in the future are explored (sections 3.5 and 3.6).

3.2. AUDIT

Audit of transfusion practice is the systematic, independent and documented assessment against defined criteria to obtain evidence to determine whether transfusion practice conforms to planned guidelines, and whether these guidelines are implemented effectively and are suitable to achieve the policy and objectives of appropriate transfusion (Last, 2000).

Given an awareness of practice variability and inappropriate use in the field of blood transfusion, audits are required to record current practice for means of information, education and benchmarking for the future (Wallis, Stainsby & McClelland, 2002). Audits often report on blood use and pre- and post-operative and pre- and post-transfusion haemoglobin levels with respect to guidelines in order to assess the appropriateness of transfusion. They provide an evidence base which can be used to inform policy revision as well as identifying areas of transfusion practice that require further input from education and guidelines. Ultimately, audits aim to contribute to improving safety and appropriateness of blood use, which is of great importance given the pressures affecting the supply of blood.

A marked change in transfusion practice has been the move away from whole blood transfusion to the use of blood component therapy as developments in blood component production and understanding physiological need have been made. A survey of clinicians' requests for whole blood was carried out in the UK in 2001 to assess the extent to which, and reasons for which, whole blood was still being used (MacLennan & Murphy, 2001). Whole blood was primarily used for neonatal exchange and paediatric surgery, and in adults, for major bleeding and in particular for post-operative bleeding following cardiac surgery that was unresponsive to component therapy generally recommended for emergency haemorrhage (MacLennan & Murphy, 2001). More than 90% of responding hospitals (58% response rate) had made no request for whole blood, though the true extent of the issue may be underestimated because users of whole blood were less likely to provide data and risk facing criticism over their practice.

The audits of red blood cell use described next represent a range of audit cycles: single audit (Bray *et al*, 2003), audit and re-audit following guideline development and implementation (Mallett *et al*, 2000), three audit cycle involving guideline development and practice reminders (Spencer *et al*, 2005), and an extensive cycle of four audits over ten years during which the study period and outcome measurements were expanded (James *et al*, 2001). Further, three audits of fresh frozen plasma use (FFP) are described. The appropriate use of FFP is of increasing interest given the impact of precautions against vCJD on the supply of fresh frozen plasma, the rise in the use of blood component types other than red blood cells and emerging evidence that casts doubt on the efficacy of treatment using FFP transfusion (Stanworth *et al*, 2004).

The only audit of red blood cell use in all clinical settings, rather than surgical settings described here is a study of a representative sample of transfused adults in India when a National Blood Policy, that encompassed strategies to encourage the appropriate use of blood, had just been introduced (Bray *et al*, 2003). The audit compared the reason for transfusion with national transfusion guidelines (NACO)[3] to assess the appropriateness of blood use. The audit did not extend to paediatric and neonate transfusions because of the difference in transfusion guidelines from adult transfusions. 74% of adult transfusions were assessed as being inappropriate; inappropriate transfusion was most commonly identified as being for unnecessary treatment of iron-deficiency anaemia and volume replacement. 92% of transfusions to patients with a haemoglobin level of at least 7g/dL were assessed as being inappropriate (Bray *et al*, 2003). The audit over-represents young males, and, because young people are less likely to be inappropriately transfused, the audit is likely to under-estimate the true extent of inappropriate transfusion. The report concludes that inappropriate transfusion is a significant issue in India.

Haemoglobin levels are commonly cited as a measure used to asses appropriateness of transfusion. Pre-operative haemoglobin levels and haemoglobin levels at the time of transfusion were measured in an audit of red blood cell use in elective surgery patients (Mallett *et al*, 2000). The results were used to develop departmental guidelines and the audit was repeated eighteen months after the guidelines were implemented. The results of the

[3] NACO: National AIDS Control Organisation, 1996, Transfusion Guidelines. The National AIDS Control Organisation, Ministry of Health and Family Welfare (India), responsible for the Indian national blood safety programme since 1992.

second audit showed that a decrease in the total number of peri-operative transfusions by 43% mostly attributable to the reduction in two-unit transfusions as the level of blood loss associated with triggering a two-unit transfusion was increased during the study period (Mallett *et al*, 2000). A significant change in departmental peri-operative transfusion practice was observed in comparable audits following guideline implementation, however, post-operative transfusion practice was largely unaffected by the guidelines although there were indications that the practice of top up transfusions had decreased.

Another prospective audit cycle of blood use in elective surgery, in this instance, specifically hip and knee replacement surgery, was carried out using three audits over a period of two years (Spencer *et al*, 2005). The study aims were to determine the proportion of patients transfused post-operatively following joint replacement surgery and again to develop guidelines for transfusion practice. Transfusion rates from the first audit were compared with regional figures in order to inform local guidelines. The new guidelines required the indication for transfusion to be recorded. This recommendation illustrates the increasing awareness of the importance of reporting the clinical reason for transfusion. Transfusion practice was audited a second time, and a third time following the issue of guideline reminders. The overall rates of transfusion for hip and knee replacements fell from 71% to 37% after the second audit and were maintained at around 40% a year later (after the third audit and guideline reminder) indicating that the reinforcement of guidelines can contribute to reducing unnecessary peri- and post-operative transfusion (Spencer *et al*, 2005).

Four audits of red blood cell use related to surgery were carried out at a large district hospital over the period of ten years: outcomes were reported for 1990, 1994, 1996, and 1999 (James *et al*, 2001). Initially, the number of units transfused and the cross-match to transfusion ratio for each surgical procedure were reviewed by the hospital transfusion committee and used to revise a maximum surgical blood order schedule (MSBOS) that contains guidelines for the number of units required for transfusion of specific surgical procedures (1990). In the third and fourth audits blood use by consultant was included, and the study period of the fourth audit was extended from three months to one year to address seasonal variation (1999). Overall the report demonstrates a sustained reduction in the amount of wasted blood, that is, blood which is requested but not used, from 1990 to 1996 but an increase in subsequent years. This trend is thought to reflect the lag phase between

changes in transfusion practice, such as ordering habits or updated MSBOS changes, and improvements in surgical techniques that reduce the need for blood. The report also identifies the lack of communication about cancelled operations between clinical teams and laboratory staff as an area to target in order to further reduce blood wastage. Thus, communication, collaboration and self-regulation are strongly implicated in improving the efficacy of transfusion practice.

Further to red blood cell audit, the study of blood component use must encompass the other blood component types in order that a complete view of transfusion practice and targets for practice change can be made. Particularly, there is compelling evidence for the need to audit fresh frozen plasma use. A recent report suggests that there are very few clinical conditions for which treatment with fresh frozen plasma has been shown to be effective (Stanworth *et al*, 2004). Further, new regulations on the supply of plasma in the UK due to the emergence of vCJD add to concerns over its use as it is a more scarce and expensive resource than years gone by. Concerns such as these prompted the study of appropriate use of FFP by clinical indication in three separate prospective audits (Chaudhary *et al*, 2005; Hui, Williams & Davis, 2005; Palo *et al*, 2006a). The audits assessed all FFP issues during the study period (one of two two-month periods, one of thirty days, and one of two years). Appropriate transfusion of FFP was reported for 29.5% of patients (Chaudhary *et al*, 2005) and 72% of units (Hui, Williams & Davis, 2005) and was considered as inappropriate where no medical indication was recorded at the point of use, where no follow up coagulation tests were done, or where dosage differed from national guidelines (Palo *et al*, 2006a). The major indications for which FFP units were appropriately issued were chronic liver disease, coagulopathy and prolonged bleeding (Chaudhary *et al*, 2005), and anti-thrombotic warfarin effect and massive transfusion with bleeding and abnormal coagulation (Hui, Williams & Davis, 2005). Inappropriate transfusion was highlighted in areas of post-cardiac surgery bleeding and bleeding associated with normal coagulation (Chaudhary *et al*, 2005), and in haematology and cardiothoracic surgery departments (Hui, Williams & Davis, 2005). The results indicate that both studies were able to determine appropriate clinical indications for FFP transfusion, which, in accordance with national guidelines, may represent areas for targeted intervention to improve practice in the future. The main diagnostic indications for FFP use reported by Palo *et al* (2006a) were circulatory diseases and the main procedures were digestive, cardiac and thoracic surgeries. Further, a major factor discussed in that report was the

methodological issues associated with the study sample in which there was a high representation of severely ill patients and the lack of information on patient indicators such as blood loss, anticoagulant use, and previous and subsequent morbidity (Palo *et al*, 2006a). A report by the same authors in the same year describes new methodology that incorporates electronic national registers of data and computer processes to effectively monitor and compare population-based transfusion practice for all blood components (section 3.6) (Palo *et al*, 2006b).

The audits of red blood cell and FFP use that were described here are evidence that continual assessment of blood use is recognised to be important especially given variations in transfusion thresholds and clinical indications which point to inefficiency in use. However, a critical appraisal of blood transfusion audits suggested that the influence of confounding factors on audit results are not always properly considered (Kanter, 2005). Further, the report found no significant efficacy of audit of transfusion as an intervention in itself on changing appropriate use of blood in any hospital-wide transfusion audit studied during the course of the critical appraisal. To fully address this issue, an appropriately designed study of the effects of audit versus non-audit intervention on the use of blood is required. In summary, blood use audits should be rigorous and frequent, and the study design and data interpretation must be carefully considered. They should be used to revise guidelines and policy and the outcomes continually reinforced to maximise effect (Joshi & Landers, 1998; James *et al*, 2001).

3.3. OUTCOME STUDIES

Descriptive studies that report outcome measures of blood use and transfusion practice such as the demographics of transfused and non-transfused patients, transfusion rates, intensity of transfusion, trends in use, and post-transfusion survival can provide useful data for planning and research proposes. Of interest are measures of cross-matched, irradiated/leucodepleted and wasted/discarded units as well as units used for all blood component types. Further, given the rising economic implications, cost-effectiveness analyses associated with transfusion are required.

Described here are two different types of outcome study: survival studies and studies of transfusion protocols. These were chosen because each evaluates the effects of the intervention of transfusion; the specific outcome measures are patient related with respect to survival and practice related with respect to transfusion protocol. Reports on post-transfusion survival generally provide a descriptive analysis of patient survival for particular groups of transfusion recipients or compare survival of patients who are and are not transfused. Reports on the effect of transfusion protocol on blood use can evaluate the effect of variations in transfusion practice and new treatment plans such as the use of restrictive versus liberal transfusion of blood.

3.3.1. Survival studies

There are two main types of survival study: one, observational studies of survival of transfusion recipients, and two, the study of the influence of transfusion on survival where a causative relationship is implied. Studies of survival rates of transfusion recipients provide baseline data for the quantity of blood transfused as well as analysis of patient variables, notably morbidity and mortality. Survival studies contribute to the evidence base regarding transfusion safety, efficacy and cost-effectiveness are used to inform the decision to transfuse based on benefit versus risk analysis (Kleinman *et al*, 2004).

Many patient and practice variables have been implicated in predicting post-transfusion survival: age, sex, volume of blood transfused, length of hospital stay, specialty of treating physician, severity of injury or illness, physiological/biochemical test results and clinical category. However, studies of transfusion and survival are intrinsically confounded due to the effects of the underlying nature or severity of the clinical condition. The severity of disease influences treatment with blood transfusion and is likely to be the dominating influence on survival regardless of transfusion status. Due to such confounding as well as bias in case selection previous studies have found it difficult to identify variables that successfully predict post-transfusion survival. For example, in a seven-year review of trauma patients who received massive transfusion, shorter post-transfusion survival was shown to be related to higher injury severity, and shorter intensive care unit and hospital length of stay, and not transfusion related variables such as the volume of blood transfused (Criddle, Eldredge & Walker, 2005).

Diagnostic case group has been hypothesised to affect post-transfusion survival: a regional, population-based study of one- and seven-year post-transfusion survival for a case mix of primary diagnoses and surgical procedures was devised to address this (Tynell *et al,* 2005). The study reported that between 1993 and 2000, one-year survival rates increased from 68% to 74%, and that post-transfusion survival was longer for surgical patients (versus medical patients) and for young, female patients, a finding comparable to the one year post-transfusion survival rate of 69% reported for a large study of post-transfusion survival in mid-western and southern America (Kleinman *et al,* 2004). Further, the report attributes variation in post-transfusion survival to variation in population demographics, clinical practice and transfusion policy which may be indicative to some extent of areas of inappropriate transfusion (Tynell *et al,* 2005).

Currently the issue of post-transfusion survival is particularly pertinent in the United Kingdom given concerns regarding the potential risk of vCJD transmission through blood transfusion. The first study of long-term survival following transfusion in the UK was carried out in northern England to quantify the number of transfusion recipients surviving long enough to be at risk of transfusion-acquired vCJD, though not to assess the effects of transfusion on survival per se (Wallis *et al,* 2004). The median survival per red blood cell unit transfused was 31 months, and was less for FFP and platelets (19 and 6 months

respectively). Patients who were older, male, transfused with more red blood cells, and who were transfused with FFP or platelets had shorter survival, as did patients in medical specialties. The overall survival rate was 68% after one year and 47% after five years, rates that are in accord with post-transfusion rates reported by Tynell *et al* (2005) and Kleinman *et al* (2004). Post-transfusion survival was shorter than previously reported for other countries, a difference that was attributed to population and clinical practice changes. The report concludes that unless many recipients subsequently have a high rate of donor exposure and the infectivity of vCJD is high, it is unlikely that transfusion recipients are at a significant risk of infection from transfused blood (Wallis *et al*, 2004). Studies such as this are essential in monitoring post-transfusion survival in the context of infection risks, and particularly given concerns regarding vCJD, in order to provide evidence that can be used to inform the decision to transfusion based on the balance of risk versus benefit.

3.3.2. Studies of transfusion protocols

Medical protocols are concerned with the rules or guidelines for the use of a medical treatment or intervention. Described in this section are studies of transfusion protocols for the use of blood component transfusion. Evidence-based and revised transfusion guidelines are essential for uniformly directing the safe and effective use of blood.

A central, determining factor in the decision to transfuse is the level of haemoglobin in the blood: specific haemoglobin levels below which transfusion is prompted are referred to as transfusion thresholds or triggers. General guidelines for transfusion quote figures for transfusion thresholds but these guidelines can vary by country, clinical context and author and are not always based on compelling or current evidence. Compliance too varies between clinicians and hospitals (Clark & Mintz, 2001). Transfusion triggers are a principal factor in studies of appropriate transfusion in compliance with protocols. In previous years a transfusion trigger of 10g/dL was accepted but there is growing evidence for a restrictive trigger of 6-7g/dL (McClelland, 2007; Clark & Mintz, 2001). The decision to transfuse at a particular threshold must take into consideration the levels of oxygen deprivation and specific clinical needs of the individual patient, for example, anaemia and oxygen

deprivation are less well tolerated in critical care and trauma patients and the elderly. As for all transfusion events the balance of risk versus benefit of transfusion to the patient must be considered (Hill *et al*, 2002; Carson *et al*, 2002). Guidelines now recognise the safety and efficacy of restrictive transfusion thresholds where the haemoglobin level at which transfusion is triggered is lower than previously endorsed.

Furthermore, transfusion practice has historically been dominated by the practice of two-unit transfusions, deemed to be the volume necessary to make any significant improvement to anaemic patients. However, the need to conserve blood and protect patients from exposure to risks associated with allogeneic transfusion is more predominant now than ever before and has prompted a move away from unnecessary, though apparently standard two-unit transfusions and a move toward reductions in allogeneic blood use in general. Studies of the impact of transfusion protocols, such as single-unit transfusions (Ma *et al*, 2005) and restrictive transfusion thresholds (Hebert *et al*, 1999a), aim to save blood and reduce recipient exposure to transfusion-related risks and are essential to informing the evidence for future transfusion practices.

Blood use in critically ill patients presents particular challenges given the complexity and clinical instability of these patients. The impact of restrictive transfusion protocols on the conservation of blood and patient outcome was assessed in a randomised control trial of red blood cell transfusion in critical care (Hebert *et al*, 1999a). In this trial all-cause mortality rates and severity of organ dysfunction associated with restrictive versus liberal transfusion protocols in the critical care setting was examined. With the restrictive protocol the transfusion threshold was a haemoglobin level of 7g/dL and with the liberal protocol the transfusion threshold was 10g/dL. 30-day mortality rates were significantly lower in less acutely ill patients and patients less than 55 years old who received transfusion according to the restrictive protocol. The report concludes that the restrictive protocol was at least as effective if not more so, than a liberal transfusion protocol, except in cases of acute cardiac disease. This conclusion may indicate that the side effects of transfusion counter any added benefit from the oxygen carrying capacity of the additional blood transfused in liberal protocols. In a report on the ten best randomised controlled trials in the area of transfusion practice in terms of relevance to or impact on transfusion practice and policy this study was

considered to be that with the biggest potential to make a significant impact on changing transfusion practice (Blajchman, 2005).

The Hebert *et al* (1999a) study was also included in a Cochrane review of transfusion thresholds and other strategies for guiding allogeneic blood transfusion (Hill *et al*, 2000). The review identified a total of ten trials relating to transfusion thresholds in which restrictive and liberal transfusion protocols were compared, and concluded that the use of restrictive transfusion thresholds was supported by the data reported for the studies included in that review. Using restrictive thresholds, reductions were made in the risk of receiving an allogeneic transfusion and the volume of red blood cells transfused without affecting mortality, morbidity, cardiac events and length of stay in hospital. The exception was for patients with notable cardiac disease (Hill *et al*, 2000).

The first published report to assess single-unit transfusion in terms of reducing blood use and maintaining acceptable haemoglobin levels was of a retrospective study by Ma *et al* (2005). To achieve a 7g/dL transfusion threshold single-unit transfusions would have been sufficient in 98% of cases (42% of cases to achieve a 9g/dL transfusion threshold), and could represent a saving of 0.82 units per patient (0.21 units per patient if a 9g/dL transfusion threshold was required). The actual haemoglobin increase for single-unit transfusions was not assessed, rather was calculated assuming that it would be half that of the increase achieved by two-unit transfusions. Nevertheless, the report concludes that, except in cases of acute haemorrhage and anaemia, a single-unit transfusion protocol could significantly improve blood use and reduce recipient exposure to allogeneic blood (Ma *et al*, 2005).

The conclusions reported by Hebert *et al* (1999) and Ma *et al* (2005) are supported by a study of the impact of a restrictive protocol for red blood cell use in intensive care in which restrictive transfusion was associated with reduced mortality and one third of transfusions were single-unit transfusions (Farrar *et al*, 2004), and by an Australian study of appropriate red blood cell use in haematology, cardiothoracics and orthopaedics that reported areas of inappropriate transfusion with reference to haemoglobin levels and concluded that one-unit transfusions were not common (Grey *et al*, 2006).

The reports described here demonstrate the impact of liberal versus restrictive transfusion protocols and one-unit versus two-unit transfusion protocols on allogeneic blood transfusion. Further, an algorithm designed to direct transfusion protocol in a novel way is described here: compliance with a transfusion algorithm for red blood cell transfusion in primary elective total knee replacement surgery has been prospectively assessed (Boralessa *et al*, 2001). Given that there was no evidence for a specific haemoglobin level at which transfusion would improve outcome, and with the knowledge that outcome is affected by blood loss, age of patient and comorbidities, as well as wide variation in practice amongst clinicians and institutions, the available transfusion guidelines were considered to be inadequate by the researchers. The transfusion algorithm incorporated the variables pre-operative haemoglobin level, volume of blood lost and crystalloid and colloid treatment, and was based on a restrictive post-operative haemoglobin level of 7g/dL. Compliance with the algorithm for transfusions on the day of surgery and for subsequent transfusions was 62% and 89% respectively. Further, the results were compared with those from a retrospective survey by the same authors. The two study populations were described as being similar but there was a significant difference in mean post-operative blood loss between transfused and non-transfused patients in the prospective study, which was not the case in the retrospective study suggesting that the decision to transfuse in the prospective study was influenced by post-operative blood loss (and hence, haemoglobin level). The transfusion rates for the retrospective study without the algorithm and for the prospective study employing the algorithm were 64% and 30% respectively. The report concludes that the algorithm can be used to reduce inappropriate transfusions, and advocates continuous audit of practices and education of staff (Boralessa *et al*, 2001).

3.4. COMPREHENSIVE, DESCRIPTIVE STUDIES OF BLOOD USE

Here the term comprehensive, descriptive study of blood use refers to a study of blood component use that encompasses a specific group of patients, typically those that are relatively straightforward to categorise. For example, described here are studies of patients undergoing major surgical operations, trauma and critical care patients, and elderly patients. Studies and routinely published reports that quantify national blood use data are also described.

3.4.1. Elective Surgery

Early studies of clinical blood use primarily addressed transfusion practice in surgical settings. A study bias towards a small range of high blood using surgical specialties and specific operations and procedures arose because these were perceived to be clinical areas of importance and relevance and because the study populations were relatively easy to define. (Stanworth *et al*, 2002). The use of packed red blood cells in surgery at a single teaching hospital was assessed not just by type of procedure but also by consultant performing the procedure and the time of transfusion in relation to surgery (Pinkerton, Seigel & Coovadia, 1993). No significant variation in blood use between surgeons at the same hospital was found, and as a result local utilisation guidelines were produced based on the transfusion practice reported by that study. However, the report did acknowledge that a wider population study would be useful for further development of guidelines, particularly given the concurrent increase in regulatory pressures at the time that were pushing for better audit of comparative blood use data.

In contrast, red blood cell use in surgery in an Australian tertiary care hospital was studied in a setting where blood component use was already being monitored and blood conservation strategies were already employed (Maxwell *et al*, 2002). The surgical events were classified using the Commonwealth Medical Benefits Schedule, a clinical classification system developed to calculate benefit payments for medical conditions, which was used as a

proxy for defining clinical case groups. Blood use and transfusion incidence for the frequently performed (>10 times in a year) surgical procedures were reported but the findings did not detail procedures that had a high transfusion rate but were not frequently performed. Further, not all surgical specialties were represented at the study hospital (for example paediatrics, obstetrics and gynaecology specialties were absent). The report acknowledges that the findings relate only to a single institution but suggests that data such as this is useful for benchmarking and resource planning if considered in conjunction with national surgical statistics relating to the number of procedures performed. Moreover, the report provides evidence of methodological approaches that could be utilised by others in future blood use studies and reveals that the issue of blood use by clinical case group is of interest and importance.

Further, a specific study of autologous blood use in elective surgery was carried out by the same group in Australia, where at the time the utilisation of autologous transfusion was still on the increase (Savoia *et al*, 2002). The findings demonstrate that patients transfused with pre-operative autologous blood donations are more likely to be transfused than other recipients: the more liberal transfusion policy and increased likelihood of anaemia due to pre-operative donation can explain this to some extent. The effect of other confounding variables such as severity and complications relating to the procedure was not assessed in this study (Savoia *et al*, 2002). Also, a 28% wastage figure for blood that was donated but not transfused is reported. While highlighting important issues regarding autologous blood donation specifically, overall the report is illustrative of the need to study blood use in various settings in order to answer a range of questions surrounding the appropriateness and effectiveness of transfusion practise as a whole.

The studies by Pinkerton, Seigel & Coovadia (1993), Maxwell *et al* (2002) and Savoia *et al* (2002) described here were single-institution studies of blood use in surgery. By contrast, the Belgium BIOMED study was a multi-centre study (63 hospitals) of all blood components (allogeneic and autologous) used in four common surgical procedures (Baele *et al*, 1998). These were two joint-related and two colectomy-related procedures defined by the Belgian classification system for medical benefits, INAMI[4]/RIZIV. As in Maxwell *et al* (2002) and Savoia *et al* (2002), this clinical classification system is related to economic medical benefits

[4] INAMI: National institute for sickness and invalidity insurance (Institut national d'assurance maladie-invalidité)

nomenclature which may be a poor proxy for clinical classification in the context of measurements in clinical practice given the different purpose for which it was devised. The BIOMED study provided valuable data on countrywide, inter-hospital variation in transfusion practice and attributed this variation to differences in transfusion practice rather than differences in the patient populations (Baele *et al*, 1998). Also, the multi-centre approach encompassed both teaching and non-teaching hospitals: the data contradicts previous thoughts that teaching hospitals transfuse more due to the inexperience of junior trainees by reporting that transfusion practices in teaching hospitals actually benefit from the current teaching and awareness of factors relating to the transfusion practice of junior doctors. This aspect echoes the findings of other audits and studies that adherence to guidelines can be improved and inappropriate transfusion reduced by continual education and the reinforcement of transfusion related policy.

The example of the BIOMED study introduces joint surgery as a notable area of blood use. Blood loss associated with total hip and knee replacement surgery can be substantial meaning that the patient may require blood transfusion as well as the use of alternative non-blood interventions (Bierbaum *et al*, 1999; Churchill *et al*, 1998; Boralessa *et al*, 2000). In some settings, pre-operative donation of autologous blood was a commonly used strategy although it has logistical, administrative and cost implications as well as clinical implications for the patient by exposing them to a risk of pre-operative and post-operative anaemia. However, a study of pre-operative and discharge haemoglobin levels and blood loss of transfused and non-transfused patients undergoing primary total hip replacement surgery concluded that more than 90% of post-operative transfusions had been routinely given without consideration for the clinical need of the patient (Boralessa *et al*, 2000). The indication for transfusion was not recorded but these findings and the lack of a transfusion protocol suggest that a significant number of transfusions may have been unnecessary.

Further, following from a lack of evidence for autologous transfusion criteria for a broad spectrum of procedures, The Collaborative Hospital Transfusion Study embarked on a multi-hospital study (5 university hospitals in the USA) of autologous red cell transfusion for primary hip and knee surgery (Churchill *et al*, 1998). The procedures were defined by the medical classification system Diagnosis–Related Groups (all coded in section DRG 209). For both knee and hip replacement procedures the study reports a significant difference between

hospitals in the number of patients pre-operatively donating blood, in the number of patients and units transfused, and the number of unused autologous units but no significant difference in number of patients who pre-operatively donated blood but subsequently required allogeneic blood in addition to autologous transfusion (Churchill *et al*, 1998). The findings echoed those of a similar study of allogeneic red cell use in total hip and knee replacement reported seven years previously in which practice variation between hospitals was described for the number of patients, but not units, transfused (Surgenor *et al*, 1991). The reports provided further evidence of the effect of practice variation on transfusion practice.

Another large-scale study of autologous and allogeneic blood use of patients undergoing total hip and knee replacement reported that overall 46% of patients were transfused (of which 66% of patients received autologous blood, 34% received allogeneic blood) (Bierbaum *et al*, 1999). 45% of pre-operatively donated autologous blood units were not transfused and 9% of patients who pre-operatively donated autologous blood also required allogeneic blood transfusion. Notably, the report highlighted that complex logistics and high costs, as well as the risk of anaemia and need for supplementary allogeneic transfusion, were associated with pre-operative autologous blood donation, and called for further research into alternative strategies to reduce or replace allogeneic transfusion, other than pre-operative autologous blood donation.

Like joint surgery, coronary artery bypass graft (CABG) surgery has also proved to be a focus for analysis of transfusion practices. The studies referred to here describe the determinants of blood use for CABG surgery and demonstrate comparative variation in transfusion practices. Blood use data for two studies carried out in two different years has been compared: the first study in 1998 included six hospitals, the second in 2000 included 32 hospitals (Boralessa *et al*, 2002). The data revealed a decrease in blood use for CABG surgery between 1998 and 2000 but also indicated wide variation in the number of patients per hospital who were transfused: in the 1998 study the number of patients transfused varied between 58% and 91% (mean 89%) and in 2000 the number of patients transfused varied between 6% and 90% (mean 53%). The decrease in blood use in 2000 reflected the introduction of blood conservation strategies (71% of hospitals had implemented a more restrictive transfusion threshold) and it is reported that blood use was improved if three or

more blood conservation strategies were in place (Boralessa *et al*, 2002). A multi-centre retrospective analysis of blood use for one medical condition and three surgical procedures included analysis of red blood cell use for CABG surgery (Hasley *et al*, 1995). The mean percentage of CABG patients transfused was 81% but variation in transfusion practice was again highlighted as the number of units transfused and the percentage of CABG patients transfused varied between hospitals. Whilst variation in blood use for the medical condition (ulcer disease) was attributable to demographic and patient variables, the variation in blood use for the surgical procedures was attributed to transfusion practices (Hasley *et al*, 1995).

Further, a relatively early, prospective study of red blood cell use and the determinants of transfusion for CABG surgery at two institutions reported overall transfusion rates of 73% (5 units per patient) at one hospital and 52% (2.9 units per patient) at the other (Goodnough *et al*, 1989). Transfusion rates and determinants varied between the hospitals studied prompting recommendations for further multi-institution audit of transfusion practice in cardiac surgery. The research group subsequently carried out a similar study of transfusion practice for CABG surgery in eighteen institutions and again variability in blood use and determinants of transfusion were reported. When the effects of patient and surgical practice variables were controlled for factors related to transfusion practice accounted for the variation in blood use (Goodnough *et al*, 1991).

The Collaborative Hospital Study group, which was described above for a study of blood use in total hip and knee replacement surgery in which comparative analysis revealed variation in transfusion practices (Surgenor *et al*, 1998), has also studied the use of blood for coronary artery bypass graft surgery (Surgenor *et al*, 1996). The study was not a comparative analysis of blood use; rather the report reveals that transfusion requirements in CABG surgery were associated with patient characteristics and the type of procedure (primary or revision, and type of conduit used for revascularisation). Further analysis of practice variation in this study population would provide useful comparative data.

What can perhaps be considered as the cornerstone of comparative analysis of transfusion practices for surgery was a study by The Safe and Good Use of Blood in Surgery (SANGUIS) group (Sirchia *et al*, 1994). Initiated by the European Commission, the SANGUIS study brought together interested parties from ten European countries, representing forty-three

different hospitals, to assess blood use for six commonly performed elective surgical procedures over a period of two and a half years. The group gathered data for the number of patients and units of each blood component transfused, use of albumin and artificial colloids, ratio of units requested to units transfused, reasons for transfusion and transfusion-related complications. Overall, the study represented 7,195 patients of whom 34% were transfused with 11,464 units of allogeneic red blood cells. Two of the six procedures studied were CABG and total hip replacement: for which 87.7% and 80.8%, respectively, of operated patients were transfused, mostly peri-operatively, with autologous and allogeneic red blood cell units (37.6% and 56.8% with allogeneic units only). Like other studies discussed previously, wide inter-hospital variation in blood use among hospitals of the same country as well as between countries was identified by the SANGUIS study. For example, in CABG and total hip replacement surgeries the percentage of operated patients transfused with red blood cells ranged from 17% to 100% and from 29% to 100%, respectively (Sirchia *et al*, 1994). This report attributes the variability not with biological factors but rather professionals' attitudes towards and consequently their practice of blood transfusion. Further, the reason for red blood cell transfusion (low haemoglobin, bleeding and volume replacement) was reported but for just 23% of transfused patients. In conclusion, the report sets out the priorities of optimising the appropriate use of blood through data analysis, guideline development and the modification of transfusion practitioners' behaviour (Sirchia *et al*, 1994).

The comprehensive, descriptive studies discussed here are examples of studies of surgical blood use that have provided insight into the use of blood in areas of particular interest such as joint and cardiac surgery and that have addressed pertinent issues such as pre-operative autologous donation and practice variation.

3.4.2. Trauma and critical care

Although elective surgery was a focus for early studies of blood use by clinical indication, interest in better understanding transfusion practices in other high-user settings such as intensive care is growing. A multi-centre study of inter-hospital variation in the number of patients transfused, the mean number of units transfused per patient, and in mean

haemoglobin levels for the critical care setting was discussed previously with respect to restrictive transfusion protocols (section 3.3.2) (Hebert *et al*, 1999a). Other studies of blood use in intensive care and trauma are discussed here.

Given that critically ill patients are adversely affected by anaemia but evidence exists to suggest that restrictive transfusion strategies have no negative effect on these patients, analysis of blood use in comparison with practice guidelines was needed to inform the evidence base for an appropriate transfusion strategy specifically for use in the critical care setting. This aim was addressed by the Audit of Transfusion in Intensive Care in Scotland (ATICS) study of blood transfusion for a sample of patients admitted to hospital intensive care units (ICU) (Walsh *et al*, 2001 and 2004). The study likely underestimated total red blood cell use by critical care patients as it did not include additional transfusions that these patients may have received in other wards once discharged from ICU. However, the findings revealed that 26% of ICU admissions, and almost 50% of red blood cell units transfused in the study were given when the patient had a low haemoglobin level without evidence of bleeding. Overall, Scottish ICU patients were estimated to use 7% of the total Scottish red blood cell supply supporting the belief that ICU patients are an important group of transfusion recipients.

Inter-hospital variation in surgery has been well-described, as illustrated by reports discussed here; furthermore, variation is also evident in the critical care setting. A study that reports the practice of red blood cell transfusion for critical care patients in Canada (TRICC: Transfusion requirements in critical care) reveals notable practice variation between hospitals even after adjustment for patient age, diagnosis and disease severity (Hebert *et al*, 1999b; Walsh & McClelland, 2003). The study also investigated the clinical indication for transfusion in these patients but only report for "acute bleeding" (35% units transfused) and "augmentation of oxygen delivery" (25% units transfused), a reflection of the advances required in the classification and analysis of blood use by clinical reason. The report concludes that the findings support a call for further research into transfusion of critically ill patients given the complexity of ICU patients' clinical status and treatment needs (Hebert *et al*, 1999b).

Evidence for variation in transfusion practice and the determinants of transfusion is largely indicative of the need for appropriate analysis, guideline development and targeted approaches to reducing inappropriate transfusion. Corwin, Parsonnet & Gettinger (2005) reported on red blood cell use in a critical care centre in which, at the time of the study, there was no specific transfusion protocol in place. The reason for transfusion was classified according to the National Institutes of Health Consensus Conference transfusion criteria that relate to physiological and biochemical factors such as haemoglobin level, cardiac output and oxygen transport rather than specific clinical conditions. In addition, two clinical case groups are listed: a broad, procedure-based group, "surgery/bleeding" and a specific medical condition, "myocardial ischaemia". Also available as reasons for transfusion are "none" and "other": 29% of transfusion events could not be attributed to an indication suggesting that the decision to transfuse was based on an arbitrary haemoglobin level rather than a physiological need for blood (Corwin, Parsonnet & Gettinger, 2005). The findings prompted a call for the development of and adherence to new guidelines.

Further to reversing anaemia in critically ill patients, transfusion is an integral part of resuscitation support for trauma patients and as such this area of clinical care makes a significant demand on the blood supply. Two studies of blood use in the related field of trauma quantified blood use and trends in transfusion of trauma patients in order to assess practice change and further, to use the data to inform guidelines for this clinical setting (Coovadia, Pinkerton & Sharkey, 1992; Farion, McLellan & Boulanger, 2007). Patients in a regional trauma unit were studied to assess the impact of a trauma specific target programme aimed at reducing blood use (Coovadia, Pinkerton & Sharkey, 1992). The data described trauma patient blood use and indicated the potential for implementing practice change. A few years later trends in blood use by trauma patients demonstrated that reductions in both the number of patients transfused and the total number of units transfused were indicative of the implementation of recommended changes in clinical and transfusion practices in this setting (Farion, McLellan & Boulanger, 2007).

The evidence describes notable variations in transfusion practice and a need for appropriate transfusion protocols in critical care and trauma settings where patients are especially vulnerable to oxygen deprivation, anaemia and haemorrhage. The appropriate transfusion threshold for critically ill and anaemic patients depends on a range of patient variables and

must always consider the balance of benefit versus risk. Further evidence of good quality is needed for different patient groups in order that practice concerns can be addressed, particularly for transfusion thresholds in the borderline range of 10g/dL to 7g/dL, in order to help direct the decision making process for the transfusion of critically ill patients (Walsh & McClelland, 2003).

3.4.3. Elderly population

One of the pressures on the blood supply discussed in section 2.2 was the growing ageing population in countries such as the United Kingdom and the United States. Here a study of blood use by an elderly population is described to illustrate the importance of the demand for blood in this specific patient group. A recently published report on blood use data for the inpatient population aged 65 years and older in the United States in 2001 is claimed to be the first systematic, population-based study of blood use in the elderly inpatient population (Anderson *et al*, 2007). In total six percent of the 635,700 inpatient hospital stays analysed were associated with blood transfusion. The highest users were aged between 70 and 84 years old, after which age blood use declined because the number of patients over this age was small and transfusion rates decrease because very elderly patients are considered less likely to benefit from the intervention. More blood was used by patients who underwent more procedures: the top procedures by mean blood use are reported to be surgeries related to cardiac, gastrointestinal and orthopaedic specialties. The top diagnoses by mean blood use are reported to be cardiac and gastrointestinal conditions. Overall, only small variations in blood use by age, sex, and ethnicity were reported. Despite complications in the way blood transfusions were recorded in the data, a methodological point acknowledged in the report, the study represents a valuable contribution to understanding clinical blood use for an elderly population with considerable significance for the future given the ageing population in America and elsewhere.

3.4.4. National studies and statistics

Studies that are restricted to specific clinical settings or patient groups, defined by ward, medical specialty or surgical procedure for example have been discussed (section 3.4.1-3.4.3). Studies that observe a whole population or an epidemiologically defined sample of a whole hospital, regional or national population are described in this section. These studies encompass a broad case mix of patients and can provide valuable quantitative data that can be used to assess the population's need for blood as a whole.

Official and often routine national statistics are good examples of population-based studies. For example, the Blood Utilisation Survey by the National Blood Strategy Implementation Group in the Republic of Ireland to the Minister for Health and Children reports data for allogeneic and autologous red blood cell use and other blood components for the whole of Ireland. In the year 2001 the transfusion practice of 69 hospitals was surveyed. The data represented 558,844 inpatients, and reported an estimated national red blood cell use of 3.75 units per patient transfused (O'Reilly, 2004). The survey also highlighted interventions that were employed at that time to address the safety and efficiency of transfusion: 73.8% of hospitals surveyed had a maximum surgical blood ordering schedule, 78.7% had a hospital transfusion committee, and 80.3% had formal transfusion guidelines for red blood cell use (O'Reilly, 2004). This study also reported a high level classification of blood use by clinical specialty revealing that 42% of red blood cell units were transfused to surgical patients, 22% to general medical patients and 16% to haematology/oncology patients. Although the clinical categories lacked specific details of procedures and conditions the report made some attempt to describe blood use by clinical case group. The importance of studying blood use by clinical case group is discussed in full in section 3.5.

A marked contribution to population blood use statistics has been made by a research team in the United States which has undertaken a series of national surveys of blood collection and transfusion activities for a large study sample that is representative of the whole country (Wallace *et al*, 1993, 1995 &1998; Sullivan *et al*, 2002 & 2007; Sullivan & Wallace, 2005; Surgenor *et al*, 1998). Prospective surveys for years 1980-1985 , 1989 , 1992 , 1994, 1997 , 1999 and 2001 reported data for measures of units (of initially whole blood and red blood cells but later all blood components) collected, discarded/outdated, leucodepleted/irradiated,

wasted and transfused. In 2001 the survey was extended to include data for cellular therapy product use in haematopoietic transplantation, reflecting growth in the range of medical conditions that can be treated with blood component transfusion (Sullivan *et al*, 2007).

The data from each year was compared with previous studies in the series, thereby enabling analysis of trends. In addition, the 1980-1985 study compared rates of transfusion between four hospitals (Surgenor *et al*, 1998). Overall the studies report an increase in transfusion rate between 1980 and 1982, followed by a levelling and constant rate between 1982 and 1985 (Surgenor *et al*, 1998), in parallel with an increase in the country's total blood supply to 1989 (Wallace *et al*, 1993); a decrease (by 3.1%, 3.3% and 5.5%) in blood supply in years 1992, 1994 and 1997 (Wallace *et al*, 1993; Sullivan *et al*, 2002); a constant average red cell units used per 1,000 population (approximately 42.8) over years 1994 and 1997 (Wallace *et al*, 1998; Sullivan *et al*, 2002); and an increase in total blood supply (10.1% to 10.4%) as well as an increase in average red cell units used per 1,000 population (5.8% to 9.9%) over latter years 1999 and 2001 (Sullivan & Wallace, 2005). Together the data provide comprehensive, quantitative data on the supply and demand of blood in the United States over a period of many years. A weakness perhaps of these studies is that no attempt was made over the years to include clinical data in light of growing awareness of the importance of understanding the clinical reasons for which blood is transfused. In the most recent of the series, the authors do refer to a need to address physician preferences regarding transfusion practices and they recognise the effect of general heightened awareness about safety issues on the supply of and demand for allogeneic blood transfusion (Surgenor *et al*, 1998).

3.5. COMPREHENSIVE, DESCRIPTIVE STUDIES RELATING BLOOD USE TO CLINCAL DATA

Large and comprehensive, descriptive studies that relate blood use to the clinical reason for transfusion are required to provide a complete view of the clinical conditions that together constitute the total use of blood in a population, and to determine the proportion of individuals in a population who are transfused. In this way the need for blood for the whole population's clinical case mix of patients can be assessed. Like the audits and surveys described previously, the ultimate aim is to inform the evidence base for blood use in order to identify variation in transfusion practices, inform policy and optimise appropriate use for the future.

Factors in the assessment of a population's need for blood should include the prevalence of specific stages and severity of disease, patients' pathophysiology and mechanisms and frequency of treatment. Suitable data sources containing valid parameters, appropriate study period and representative study population have been cited as being required in order to provide a clinically relevant framework within which to study the patients who have the greatest need and who will gain the most benefit from receiving transfusion.

As has been described in previous sections, the relevant evidence base typically reports for specific patient groups or biased case mix groups, for single or few institutions that are representative of local demand for and use of resources, and that are not representative of a whole country or sample population. Here the noteworthy population based reports of blood component use for the full spectrum of patients who have conditions or undergo treatments that may require transfusion described by clinical categories that represent patients' underlying reasons for transfusion requirement are discussed. A thorough, albeit non-systematic review of published reports was carried out to identify studies of the transfusion of red blood cell units in relation to clinical information pertaining to the transfused individual. The methods used to identify studies fall short of the required standards of Cochrane systematic reviews (Figure 3.1) (Higgins & Green, 2006). However, the process did employ search and refinement methods, forward citation searches, and literature recommended by experts in the field, to develop a specific search strategy with assistance from specialists at SNBTS and university libraries (Table 3.1). The inclusion

criteria for this review were studies of red blood cell use for a well defined population or appropriately selected and described sampled of a population in which an attempt had been made to relate transfusion data to clinical information. A specific review of the methodology of these quantitative, population based studies of blood component use with specific reference to well-defined clinical categories was undertaken (sections 3.5 and 3.6).

Figure 3.1 Literature citation selections

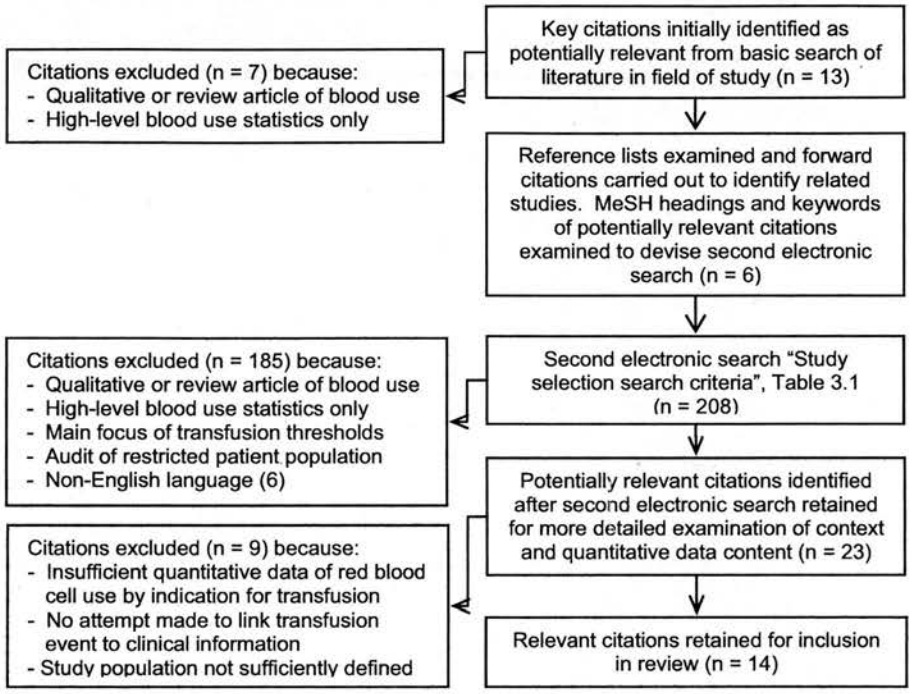


Table 3.1 Study selection search criteria

Search *	Search term (number of citations)
1	Blood transfusion/sn, ut (1,550)
2	Blood component transfusion/sn, ut (141)
3	Erythrocyte transfusion/sn, ut (254)
4	*Blood banks/sn, ut (81)
5	Surgical procedures, operative/ (43,456)
6	Hospitals/ (81,598)
7	(or/1-3) and (or/4-6) (208)

* Ovid Medline, 1966 to February Week 2 2006 (10th February 2006)

Table 3.2a **Epidemiological data and methodological information reported by studies under review**

Study	Study Setting	Study Population	Blood Component	Patients Discharged	Patients Transfused	Units RBC Transfused
Friedman, 1979	USA - 300 Short term, Non-federal, General hospitals (>1000 patients annually) representing a country. One year (1974)	Sample of all transfused patients in hospital discharges	Whole blood + RBC	2,008,230	92,815	289,414
Chiavetta, 1996	Canada - 45 Teaching & non-teaching hospitals within one province. One year (Sept 1991 - Aug 1992)	All transfused discharges, each included more than once	RBC	439,373	26,611	101,116
Zimmerman, 1997	Germany - 1 Acute care University Teaching hospital: high blood use surgery. Two years (Jun 1994 - May 1995)	All records in blood bank for which there is a discharge record	RBC, FFP, Platelets	100,497	6,590	28,440
Zimmerman, 1998	Germany - 1 Acute care University Teaching hospital representing country acute paediatrics. 27 months (Jun 1994 - Sept 1996)	All records in blood bank for which there is a discharge record	RBC, FFP, Platelets	Not stated	847	2,869
Mathoulin-Pelissier, 2000	France - 175 Teaching/other hospitals randomly sampled from 1,056 hospitals in a region. Ten months (Mar 1997 - Dec 1997)	Sample of all transfused patients, each included once	RBC	Not stated	3,206	6,831
Titlestad, 2001 & 2002	Denmark - 2 Tertiary Care, University hospitals (one limited specialties). Two periods of one year (1997 & 1998)	All records for all inpatients registered by blood bank	RBC; FFP; Platelets	43,698	9,999	59,235
Lim, 2004	Korea - 1 Tertiary Care University Teaching Hospital serving city suburb. Six years (Mar 1996 - Feb 2002).	All discharged adults transfused with any blood component.	RBC, FFP, Platelets	181,730	31,308	171,916
				Discharge Records	**Transfusion Records**	
Cook, 1991	USA - 12 State/Federal/profit/non-profit hospitals from one whole region. One year (1986)	Sample of all medical records of patients transfused	RBC, FFP, Platelets	2,579	Not stated	10,506
Syrjäla, 2001	Finland – 1 Tertiary Care, University hospital. One year (1998)	All transfusion records recorded in computer register	RBC, FFP, Platelets	Not stated	9,343	45,712
				Units Issued	**Units Transfused**	
Stanworth, 2002	London & SE England - 62 of 77 Trusts/hospitals in London and SE England. One year (Apr 1997 - Mar 1998)	All RBC units issued and transfused by blood bank	RBC	610,676	594,810	594,810
Wells, 2002	Northern England - 18 hospitals in a region (central Newcastle). Two study periods of 14 days (Oct 1999 and Jun 2000)	All patients who received an RBC transfusion	RBC	Not stated	9,774	9,774
Wallis, 2006	Northern England - 18 hospitals in a region (central Newcastle). Two study periods of 14 days (May and October 2004)	All patients who received an RBC transfusion	RBC	9,053	9,003	9,003
Vamvakas, 1994	USA - 4 Medical centre & State/Federal/community hospitals serving a county. 3 years (1989-1992); data collected quarterly	All transfused inpatients	RBC, FFP, Platelets	Not stated	Not stated	Not stated

Table 3.2b Epidemiological data and methodological information reported by studies under review

Study	Classification System	Source Data Files	Method of Attribution	Additional Methodology/Epidemiology
Friedman, 1979	CPHA+ List A Hospital Diagnosis Groups / H-ICDA++	Hospital Patient Data combined with Case Abstracts	Categorised on basis of diagnosis explaining hospital admission	Results by both DRG and Major Diagnostic Category
Chiavetta, 1996	ICD*-9 / BDC** & CCP†	Medical records plus blood component information added via computer protocol	No indications due to coding difficulties. Diagnostic data direct from records	Demographic data collected direct from discharge records
Zimmerman, 1997	ICD-10 / BDC	Blood Bank Software System linked to Standard Discharge Abstract Database	Direct assignment of diagnosis from Standard Discharge Abstract Database	Demographic data collected and reported
Zimmerman, 1998	ICD-9 / BDC	Hospital Transfusion Records and Medical Records	Full methods described in Zimmerman, 1997[7]	Paediatric blood use: recipients of transfusion are <18yrs
Mathoulin-Pelissier, 2000	ICD-10	Medical charts (clinical and transfusion data) or verbally from physician	Indication for transfusion obtained directly form source records	Sampling considers probability of each recipient being included in final sample
Titlestad, 2001 & 2002	ICD-10	Blood Transfusion, Diagnosis and Procedures, Clinical Biochemistry	Separate tables were designed for specific pieces of data linked via patient ID	Transfusion event linked to the subsequent admissions episode
Lim, 2004	ICD-10 / BDC	Computerised Blood Bank and Discharge Records	Surgical and medical data directly available but attribution process unclear	Demographic data collected
Cook, 1991	DRG‡	Patients' Medical Records	Query from source medical history, principal diagnosis and surgical status data?	Systematic sampling for study population. Demographic data collected and reported
Syrjäla, 2001	DRG	Routine Patient Databases and Blood Bank Computer Register	Combined using SAS programming tools to make online analytical processing file (OLAP)	Compiled monthly. Emphasis on providing data on costs of transfusion
Stanworth, 2002	Clinical specialty	Computerised Blood Bank Registers (see note on additional methodology)	Review and extraction by Clinical Research Studies Coordinator/Hospital Staff	For laboratories without correct software, data from finance/technology departments
Wells, 2002	Specialty/ Authors' categories	Blood Bank Records – data abstracted directly onto pre-printed survey form	Investigator classified the stated indication as reported on blood bank records	All gastrointestinal: subdivision of medical. Recipient age and gender of reported.
Wallis, 2006	Specialty/ Authors' categories	Blood Bank Records – data abstracted directly onto pre-printed survey form	Investigator classified the stated indication as reported on blood bank records	Repeat of Wells *et al*, 2002 with focus on medical indications
Vamvakas, 1994	Authors' categories	Medical Records and Division of Transfusion Medicine Blood Records	Records reviewed by medical/surgical indication then specialty (surgical if surgery during admission)	Recipient age and gender collected but not reported. Rates by age reported

Note1: Study is referenced by first author and year of publication. + CPHA: Commission on Professional and Hospital activities; ++ H-ICDA: American Hospital adaptation of International Classification of Diseases; * ICD: International Classification of Diseases; ** BDC: Broad Diagnostic Categories; † CCP: Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures; ‡ DRG: Diagnosis Related Groups. Note2: Information Titlestad *et al*, 2001 and Titlestad *et al*, 2002 is combined because same methodology used and same results reported.

Fourteen studies were identified for inclusion in the review (Tables 3.2a&b). These studies were carried out in France, Germany, Denmark, Finland, United States, United Kingdom and Korea, the earliest of which was published in 1979 (Friedman, Burns & Schork, 1979). Studies reflect changes in transfusion practice in response to emerging pressures on blood services over the intervening years. The study by Friedman, Burns & Schork (1979) proved to be a pinnacle paper of its time and in its area of research, and prompted many questions about future research requirements in order that studies provide sound evidence on the clinical use of blood for transfusion. In 1991 the results of the first regional study of blood use by clinical case group in the United States were published (Cook & Epps, 1991). Those findings supported Friedman *et al*'s suggestion that a sizable proportion of transfused blood could be linked with patients diagnosed with malignant neoplasms and added evidence for the high use of blood for surgical interventions. Over the years a number of studies have contributed to the evidence for high blood use in the areas of malignant and haematological disease (Titlestad *et al*, 2001 & 2002; Syrjäla *et al*, 2001; Chiavetta *et al*, 1996; Mathoulin-Pelissier *et al*, 2000; Zimmerman *et al*, 1997 & 1998; Lim *et al*, 2004; Wallis, Wells & Chapman, 2006) and increasingly findings suggest that surgical interventions now use less blood (as a proportion of total blood use) (Wells *et al*, 2002; Vamvakas & Taswell, 1994; Mathoulin-Pelissier *et al*, 2000; Stanworth *et al*, 2002; Zimmerman *et al*, 1997; Wallis, Wells & Chapman, 2006). Where blood use for surgical events is described the clinical areas frequently reported are gastroenterology, cardiology/cardiothoracics, orthopaedics and general surgery (Wells *et al*, 2002; Chiavetta *et al*, 1996; Stanworth *et al*, 2002; Titlestad *et al*, 2001; Wallis, Wells & Chapman, 2006).

Many of the studies identified here were the first in their region or country to carry out this type of research on a large or population based scale. The study by Zimmerman *et al* (1998) was the first to analyse data of this nature for a population of children and adolescents, and not just for red blood cells but also for fresh frozen plasma and platelets. Blood use by age is also described for studies that identified increasing use in the elderly population, although definitions of age bands varied between studies (Wells *et al*, 2002; Vamvakas & Taswell, 1994; Mathoulin-Pelissier *et al*, 2000; Wallis, Wells & Chapman, 2006). Studies have benefited from developments in information technology by employing computerised registers of data and record linkage to considerably ease the handling of large volumes of routinely collected data (Titlestad *et al*, 2001 & 2002; Syrjäla *et al*, 2001; Zimmerman *et al*, 19997 & 1998; Lim *et al*, 2004;

Stanworth *et al*, 2002). One study specifically addressed the use of computerised registers and developed processes for the automated generation of reports of blood use by clinical category (Titlestad *et al*, 2002).

In the following sections three important aspects of study methodology are reviewed. These areas are the study setting and population, clinical data and classification systems, and source data and record linkage processes (Table 3.3). Findings quoted in the following sections are included in Tables 3.2a and 3.2b that summarise the relevant information about the studies reviewed. Aspects of methodology affect the interpretation and comparability of reported data and reveal areas where further development of methods is required in order to provide useful and meaningful data in the future.

Table 3.3 Information extracted for review: aspects of study methodology

Study Setting and Population (Section 3.5.1)	Clinical Data and Classifications (Section 3.5.2)	Source Data and Record Linkage (Section 3.5.3)
▪ Study setting (i.e. hospital, ward)	▪ Surgical/procedural system	▪ Source records
▪ Geographical catchment	▪ Medical system	▪ Source of clinical indication
▪ Population denominator	▪ Categories reported	▪ Method of attribution of transfusion event to clinical category
▪ Age restriction	▪ Level of detail of categorisation	
▪ Study period	▪ Percentage of total units not categorised or reported	▪ Timeframe of attribution
▪ Blood component type(s)	▪ Units used by clinical category	▪ Timeframe for clinical relevance
▪ Total number of units reported		

3.5.1. Study setting and population

The studies included in this review encompassed a broad range of hospital settings including teaching, non-teaching, tertiary care, State/Federal, district/general and university hospitals, and included between one and 300 hospitals per study. Blood use in teaching hospitals was thought to be higher than in non-teaching hospitals because of the relatively inefficient prescribing practices of inexperienced, trainee doctors; conversely however teaching hospitals may in fact transfuse less blood because of the raised awareness of newly trained doctors, educated in current guidelines and available alternatives and blood conservation strategies. The geographical catchment areas of study settings were hospital,

city, county/regional, country-wide and in some cases was not-stated. One study in a paediatric hospital had a maximum inclusion age of 18 years (Zimmerman *et al*, 1998), one study included adults over the age of 18 years only (Lim *et al*, 2004), and the other studies reported no age criteria. The study period ranged from 14 days to six years with the most commonly reported period being one year. Five studies reported red blood cell use alone (Chiavetta *et al*, 1996; Mathoulin-Pelissier *et al*, 2000; Wells *et al*, 2002; Stanworth *et al*, 2002; Wallis, Wells & Chapman, 2006), eight reported data for red blood cells, platelets and fresh frozen plasma (Titlestad *et al*, 2001 & 2002; Vamvakas & Taswell, 1994; Syrjäla *et al*, 2001; Zimmerman *et al*, 1997 & 1998; Lim *et al*, 2004; Cook & Epps, 1991), and one reported on whole blood and red blood cell units (Friedman, Burns & Schork, 1979). The number of red blood cell units studied and reported as used ranged from 6,831 (Mathoulin-Pelissier *et al*, 2000) to 594,810 (Stanworth *et al*, 2002); 2,869 used red cell units were studied for the paediatric population reported by Zimmerman *et al* (1998).

For all but three studies the study population comprised all patients transfused within the specified study period and setting, be that at a hospital, regional, or national level; the remaining three studies collected data from a sample of the study population's transfusion records (Friedman, Burns & Schork, 1979; Mathoulin-Pelissier *et al*, 2000; Cook & Epps, 1991). Across reports study populations were expressed in terms of patients (Titlestad *et al*, 2002; Chiavetta *et al*, 1996; Mathoulin-Pelissier *et al*, 2000; Zimmerman *et al*, 1997 & 1998; Lim *et al*, 2004; Friedman, Burns & Schork, 1979), records (Syrjäla *et al*, 2001; Titlestad *et al*, 2002, Cook & Epps, 1991) or units (Titlestad *et al*, 2001; Wells et al, 2002; Stanworth *et al*, 2002; Wallis, Wells & Chapman, 2006), although the definitions for transfused patients, transfusion events, and records or episodes of clinical care varied between studies. In all reports there was a lack of comprehensive description of the denominator population from which the study population was obtained. The variations in study settings and composition of study population contribute to the explanation for why there was variation between institutions in the distribution of blood use to clinical case groups (Tables 3.4a-c). How far these studies are representative of their wider populations and therefore appropriate for directing national guidelines on blood resource planning should be questioned, in particular for the four studies based in a single institution where potentially the reported blood use data is not representative of all transfusion and clinical events for the population served by the blood services in that area (Syrjäla *et al*, 2001; Lim *et al*, 2004; Zimmerman *et al*, 1997 & 1998).

3.5.2. Clinical data and classification systems

The previous section highlighted the importance of well-defined study populations and denominator information for full and useful interpretation of blood use data. This section focuses on aspects of the clinical data, namely the classification systems used to record it and the clinical case groups for which blood use was reported. The findings reveal disparate distributions of used blood component units between clinical case groups, variation which may in part be a reflection of the differing methods employed.

The data recorded in clinical records represents a range of clinical classification systems for coding medical conditions and surgical procedures. In summary the classification systems used to record medical conditions were the International Classification of Disease (ICD)-9 and/or ICD-10 (individual codes and Broad-Diagnostic Categories (BDC)) (Zimmerman *et al*, 1997 & 1998; Lim *et al*, 2004; Chiavetta *et al*, 1996; Mathoulin-Pelissier *et al*, 2000; Titlestad *et al*, 2002), and variations of Diagnosis-Related Groups (DRG) (Syrjäla *et al*, 2001; Friedman, Burns & Schork, 1979; Cook & Epps, 1991). One study described automatic classification by a process called "NordDRG grouper" which uses DRG classifications that map diagnostic data to ICD-10 and surgical data to the Finnish NCSP[5] classification (Syrjäla *et al*, 2001; CIHI, 2004). Only one other study reported the classification system used to define and report surgical operations and procedures: the Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) (Chiavetta *et al*, 1996). Four studies relate clinical case group definitions to medical specialties specifically (Titlestad *et al*, 2001 & 2002; Wells *et al*, 2002; Wallis, Wells & Chapman, 2006), and a further study classifies blood use by clinical specialty/directorate (Stanworth *et al*, 2002). In some cases the process of classification to categories is unclear, and in these instances it is assumed that the decision on how to classify clinical information was determined by the researchers on an *ad hoc* basis.

Studies also vary in the level at which clinical codes or case groups were grouped and in the types of categorisation reported and because of this the reported blood use data was difficult to compare (Table 3.4a-c). Three studies reported a specific surgical or medical classification of red blood cell use: transfusion events attributed to the surgical case group accounted for 41-51% of total red blood cell units used during the study period (Titlestad *et al*, 2002; Wells

[5] NCSP: NOMESCO Classification of Surgical Procedures

et al, 2002; Stanworth *et al*, 2002). However, in only one of these studies was 100% of used red blood cell units classified (Titlestad, 2002) with unclassifiable or unreported data, or units attributed to "other" categories equalling 8% and 14% for the other two studies. In two reports transfusion events that were attributed to the medical case group accounted for a higher percentage of total red blood cell units used during the study period than surgical blood use did: 52% (Wells *et al*, 2002) and 53% (Titlestad *et al*, 2002) versus 36% (Stanworth *et al*, 2002) (Table 3.4a). The higher percentage of medical blood use may be explained by methodology that biases the classification of blood use towards the medical case group. In the study by Wells *et al* (2002) all gastrointestinal conditions were categorised into the medical case group whereas gastrointestinal conditions in other studies are included in both the surgical and medical case groups. Titlestad *et al* (2001 & 2002) link blood use with clinical data in the admissions episode subsequent to the admission during which the transfusion took place and hence blood use at the time of a surgical procedure may be misclassified as a subsequent medical indication. Some studies further described red blood cell use by sub-classification of medical and surgical case groups but not all sub-classifications were reported (2% to 74% of relevant blood use was omitted from medical classifications (Titlestad *et al*, 2002; Wells *et al*, 2002; Vamvakas & Taswell, 1994; Chiavetta *et al*, 1996; Lim *et al*, 2004; Zimmerman *et al*, 1997; Cook & Epps, 1991), and 36% to 62% from surgical classifications (Titlestad *et al*, 2002; 6, Friedman, Burns & Schork, 1979; Cook & Epps, 1991). Incomplete reporting further impaired the ability to compare and contrast results between studies.

Table 3.4a Percentage of total blood use reported as surgical/medical classification

Study	RBC units transfused	Surgical classification	Medical classification	Other classification†
Titlestad, 2002	59,235	47.0	53.0	0
Wells, 2002	9,774	40.7	51.6	7.7 *
Stanworth, 2002	594,810	51.2	36.0	12.8 **

Note: Study is referenced by first author and year of publication. † Other classification: units not accounted for under major surgical/medical classifications. *6.3% of reported units transfused for obstetric or gynaecological indications and no clinical data available for 1.4%. **12.8% described as being transfused for "combined" directorates or specialities.

Table 3.4b Percentage of blood use reported by sub-category of medicine for diagnostic classification systems

Study	Clinical classification system	RBC units used for medical classifications	Neoplasm	Blood & Blood-forming organs	Injury & Poisoning	Digestive System	Circulatory System	Pregnancy& Childbirth	Musco-skeletal & Connective Tissue	Infectious Disease	Genito-urinary System	Respiratory System	Nervous System	Congenital Disorders	Unreported †
Cook, 1991	DRG	10,506	16.0	.	14.0	17.0	24.0	.	6.0	.	.	.	.	.	24.0
Chiavetta, 1996 *	ICD-9	101,116	26.7	4.9	13.4	17.9	16.2	2.3	5.4	.	3.8	2.8	0.4	.	6.2
Zimmerman, 1997	BDC	28,440	27.0 ‡	2.3	6.0	11.4	22.9	0.3	2.4	3.1	2.2	2.3	1.0	.	19.1
Zimmerman, 1998*f*	ICD-9/BDC	2,869	23.9	9.8	.	.	.	11.3	.	.	.	.	.	34.3	20.7
Mathoulin-Pelissier, 2000	ICD-10	6,831	42.0	4.0	16.0	14.0	8.0	1.0	6.0	2.0	4.0	1.0	<1.0	<1.0	<2.0
Wells, 2002 * #	Specialty	5,047	.	15.5	.	10.8 §	.	.	.	.	.	.	.	.	73.7
Stanworth, 2002 *	Specialty	214,266	52.6 [a]			2.2					1.2				44.0
Lim, 2004	ICD-10/BDC	171,916	28.2	1.3	19.6	12.9	9.1	7.4	7.2	2.5	3.4	2.0	1.5	1.7	3.2

Note1: Study is referenced by first author and year of publication. Note2: Sub-categories reported in table defined for comparison specifically in this study. * Studies also included in Table 3.4c: "Percentage of blood use reported by sub-category of surgery for surgical classification systems". § Includes all "Gastrointestinal" indications. † Unreported quantifies the percentage of units classified as medical but units assigned to other sub- categories not described in report or described as other sub-categories not included in this Table. ‡ Not including haematological neoplasms. *f* Study population is children under age of 18 years only. [a] All haematology and oncology case groups in study including "Haematology & general medicine" and "Oncology & radiotherapy". # Updated study Wallis *et al* (2006) could not be summarised using classification defined in this table: 46.7% Anaemia, 29.5% Haematology, 22.3% GI bleeding and 1.5% Neonatal (n=5,558 red blood cell units used for medical indications)

Table 3.4c **Percentage of total blood use reported by sub-category of surgery for surgical classification systems**

Study	Clinical classification system	RBC units used for surgical classifications	General Surgery	Digestive System / Gastroenterology	Cardiac	Cardio-vascular	Cardio-thoracic / Respiratory	Obstetrics & Gynaecology	Vascular	Orthopaedic / Muscoskeletal	Urology	Neurology	Unreported †
Chiavetta, 1996 *	CCP	88,101^	.	23.0	.	18.2	4.2	.	.	16.8	3.0	2.2	32.6 *ƒ*
Titlestad, 2001 §	ICD-10	33,661	.	.	5.7	49.7		6.4	.	.	21.0	.	17.2 [a]
Stanworth, 2002 *	Specialty	304,519	26.6	.	.	.	15.9	10.2	<1.0	19.9	5.0	<1.0	<22.4
Wells, 2002 *	Specialty	4,594	9.6	.	.	.	6.1	13.3	4.6	13.9 ‡	2.6	1.2	62.0
Wallis, 2006	Specialty	3,001	13.3	16.5	.		15.7		11.7	18.9	6.4		17.6 [#]

Note1: Study is referenced by first author and year of publication. Note2: Sub-categories reported in table defined for comparison specifically in this study. * Studies also included in Table 3.4b: "Percentage of blood use reported by sub-category of medicine for diagnostic classification systems". ^ 101,116 RBC units used in study (all units described by medical case group in Table 3.5.4) minus 13,015 RBC units used by patients who were coded correctly but did not undergo a surgical procedure. § Not full results reported in study: data in table only for the shared specialties at both hospitals analysed. † Unreported quantifies the percentage of units classified as surgical but units assigned to other sub-categories not described in report or described as other sub-categories not included in this Table. ‡ Orthopaedic case-group in this study includes trauma. *ƒ* Includes 12.9% RBC units that were not attributed to surgical case groups. [a] Includes RBC units transfused to paediatric and nephrology case groups. # All trauma use

3.5.3. Source data requirements and record linkage

The previous section describes aspects of the clinical data, the classification systems used to record it and the clinical case groups for which blood use is reported, concluding that apparent practice variation may be in part due to the variation in study methodology employed. This section explores further the methods used to link transfusion events to patients' clinical information and further, describes the challenges related to this particular and crucial aspect of methodology.

In the studies identified here, the piece of clinical data that was inferred to be the underlying reason for the transfusion event was either directly interpretable from the source records (transfusion and clinical registers, or survey form) or had to be deduced by linking data sources. In five studies the former was the case: the clinical case group to which blood use was attributed could be directly ascertained from the single source record (Mathoulin-Pelissier *et al*, 2000; Cook & Epps, 1991; Wells *et al*, 2002; Stanworth *et al*, 2002; Lim *et al*, 2004), though in only one report did the methods explicitly state that the clinical case group or particular reason was reported in the source record (Mathoulin-Pelissier *et al*, 2000). In nine reports the process of data linkage and attribution of transfusion event to clinical case group was carried out automatically by computerised procedures (Titlestad *et al*, 2001 & 2002; Vamvakas & Taswell, 1994; Syrjäla *et al*, 2001; Chiavetta *et al*, 1996; Zimmerman *et al*, 1997 & 1998; Lim *et al*, 2004; Friedman, Burns & Schork, 1979). For some of the studies that employed computers the methods used to infer a relationship between a transfusion event and clinical data were explained to some degree (Titlestad *et al*, 2002; Vamvakas & Taswell, 1994; Zimmerman *et al*, 1997 & 1998; Friedman, Burns & Schork, 1979); however, in the remainder the method was unclear, was described in insufficient detail or was not disclosed, and therefore reports did not convey accurately the decision making process (Titlestad *et al*, 2001 & 2002; Syrjäla *et al*, 2001; Chiavetta *et al*, 1996; Lim *et al*, 2004).

As well as varying in study period, studies reviewed here vary in their approach to defining the time frame of association of clinical data with transfusion events. One study collected data for the initial 24 hours after the first record of transfusion (Mathoulin-Pelissier *et al*, 2000). Another linked transfusion events to the hospital admission episode subsequent to

transfusion (though the method used if patients had only one admission was not specified) on the presumption that the clinical reason for transfusion was related to the medical circumstance necessitating readmission (Titlestad *et al*, 2002).

3.5.4. Overview of review of published literature for comprehensive, large-scale, descriptive studies of blood use by clinical case group

In conclusion, studies of blood use by clinical reason typically vary in study size, methodology, comparability and bias, but where available, large-scale studies with common methodology and those that embrace collaborative and multi-centre approaches make a most useful contribution to the evidence base.

Studies that report blood use data for specific patient groups or settings are restricted in their ability to inform the transfusion needs of the wider, general population case mix., whereas large-scale or population based studies have the potential to provide comprehensive and representative data for a broad case mix of patients. The latter provide a national picture of supply and demand, reveal areas of practice variation, allow for analyses of trends in population demographics and clinical and transfusion practice), and provide data about the transfusion needs of a whole population. Consequently the data can be used to inform future resource planning by blood services. Even considering variations in methodology the review of studies described here demonstrates apparent variation in transfusion practice, echoing findings reported by other descriptive studies of blood use (section 3.4) and by routine, national data that demonstrates that large variations in use exist not just between countries of differing socioeconomic development status but also between and within comparable populations (WHO, 2004). In order to optimise appropriate blood use, improvements to prescribing behaviour, policy and audit, and ultimately, in study design and interpretation of blood use data are required.

3.6. REFLECTIONS ON METHODOLOGY OF COMPREHENSIVE DESCRIPTIVE STUDIES RELATING BLOOD USE TO CLINICAL INFORMATION

The reports of red blood cell use by clinical case group that are described in section 3.5 suggest variations in blood use by setting for a range of clinical indications. Some of the studies described here were considered in the first world-wide, comparative view of studies reporting clinical use of blood (Cobain, 2007). That review examined the demographics of transfused populations and the clinical indications for which patients were transfused, concluding that there were notable similarities between countries for transfusion by age and gender; differences in the types of blood components available, prevalence of disease and treatment protocols meant that the clinical indications for which patients were transfused varied (Cobain, 2007). The methodology of individual studies was also cited as a contributory factor to the differences identified.

Together, the studies discussed previously illustrate particular methodological issues that are central to appropriate analysis of blood use by clinical case group. These are: definition of study population, coding of clinical data and classification of clinical case groups, and the methods used to link blood use to clinical case groups. Variability in the methods of these studies prevents useful aggregation, comparison or interpretation of results. The challenges of denominator and study populations, the variations in diagnostic and surgical classification systems and clinical categories reported, the problems regarding linkage of transfusion events to clinical data, as well as, crucially, the variation in terminology and definitions, suggest important areas for development of improved epidemiological methods for blood use research. This section highlights the developments needed in research methods to ensure studies are conducted appropriately and effectively in the future.

Accurate and meaningful reporting of clinical data in patient records is essential as it affects the identification and extraction of relevant clinical data to which blood use can be attributed. The type of clinical data available may also affect the researchers' decision regarding how to classify it into clinical case groups, and subsequently which clinical case groups to report. There are numerous coding conventions and classification systems available, many of which are illustrated by the range of studies described in section 3.5. For example, the International Classification of Disease (ICD) system is a recognised, standardised tool that enables

meaningful, comparative analysis of diagnostic information across time and setting. Some studies reviewed here used a variation of the ICD system called Diagnostic-Related Groups, originally an American adaptation now used by other countries that clusters ICD codes (along with patient age, sex and discharge data) into patient categories that are similar clinically as well as in terms of resource use (ISD, online; CIHI, 2004). This type of classification system was originally developed for, and used widely to determine the cost of a patient's care for medical billing, but its usefulness has been extended to encompass the classification and reporting of clinical data in other contexts. The results of studies that use ICD codes or DRG classifications are considered to be comparable because of the similarity in structure between the two classification systems (CIHI, 2004). Classification systems that are economic coding systems currently used by insurance companies and in the assessment of medical benefits (rather than having been developed further such as ICD or DRG have been) may provide readily available and accessible clinical data but could be a poor proxy for clinical classification when used in the context of measurements of clinical practice. Universal and clinically sound coding systems that enable comparability of coded data are the ideal and future studies should strive to achieve this wherever possible.

The source of data is a particular issue because it affects the method used to attribute blood use to the appropriate clinical indication that explains transfusion. There is marked variability in data sources utilised by the studies reviewed here in that data was sourced from one or a combination of the following: blood bank records, hospital transfusion records, clinical registers, patient case notes, and specific survey forms. In general, existing, routinely collected health services registers provide large amounts of structured, comparable data for analysis and, where effectively governed by quality management, are likely to do so accurately. These are a useful source of data for healthcare research which more studies might consider for future analysis. The role of electronic data registers and use of computer methods for data extraction, linkage and analysis is emerging as a major requirement for progress in timely and reliable research of clinical blood use (Palo *et al*, 2006b; Grey *et al*, 2006).

Routine data on the clinical condition that necessitates the use of blood is rarely recorded adequately, if indeed at all, in blood bank records or patient case notes. Consequently, attempts must be made to infer this information from data recorded in clinical registers, or

be prospectively collected by survey specifically developed for the study. In the former case each transfusion event must be linked to the relevant piece of information in the clinical register representative of the correct period of clinical care during which the patient was transfused. This process however is particularly difficult, complicated by the large amount of data contained in multiple, potentially relevant transfusion and clinical records, and because of the complexities of interaction between surgical and diagnostic data contained in clinical records.

The method used to link a transfusion event to a clinical case group should ideally reflect 1) the nature of the surgical and diagnostic data in recipients' clinical records, 2) the potential for the transfusion event to be linked to multiple records of clinical data, and 3) the time frame that links the transfusion event with clinical data pertaining to a relevant period of clinical care.

In the literature reviewed, little reference was made to the time frame used to link a transfusion event with the relevant period of clinical care thereby making it difficult to understand the period of study observation relative to patients' clinical history. Within the study period of most studies identified here, recipients of all ages, stages of disease, and complexity of surgical intervention were observed. Most studies examined blood use for a fixed window of time on a record by record basis rather than on a multiple record basis or at the patient level, and there was never reference to whether historical clinical data was considered as a requirement or was even available. In future, studies might consider studying blood use for a single episode of care (for example appropriate for elective surgical intervention) or for a significant fixed time period such as one year, but which incorporates as much data as possible that is relevant to each patient. For patients with chronic or recurring conditions it may be more appropriate to study blood use for the patients' lifetime or for the period from first inpatient admission to time of death, implicating survival and quality of life analyses.

The variations in methods described here and in section 3.5 reflect the complex nature of research in this area of transfusion practice. Careful consideration and clear definitions are needed as to what constitutes a transfusion event or record of clinical care and what the appropriate clinical categories are. Also, the time frame used in the study to link transfusion

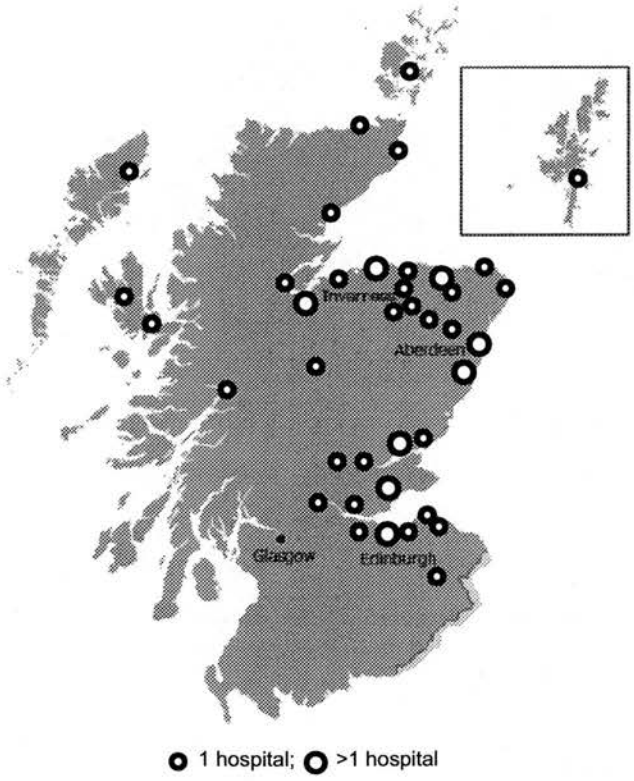
events with clinical data, the relevant period of clinical care, and their effect on data interpretation, should be defined and reported. Taken together, the challenges of variation in classification and reporting of clinical case groups, the relevance of study population and study period, and the issues related to linking transfusion events to clinical data suggest important areas for development of improved epidemiological methods for blood use research.

4. MATERIALS

4.1. STUDY POPULATION

The study utilises data collected for the Scottish Transfusion Epidemiology Project feasibility study. The data comprises routinely collected blood bank transfusion records and clinical data for patients treated during the year 2000 in all Scottish hospitals that were served by a blood bank operated by the Scottish National Blood Transfusion Service (SNBTS) which utilises the Progesa blood bank computer system (Progesa, MAK-Systems, Paris) (Figure 4.1). The denominator population for clinical data was all SMR01-CD records in the year 2000 for hospitals in the study population.

Figure 4.1 **Hospitals that have Progesa blood bank transfusion day records (SNBTS) and are included in the study dataset**



4.2. SOURCE DATA

4.2.1. Transfusion record data

Blood banks store records of information about tests performed on patients' blood samples as well as records of the assignment of blood component units created when blood component units are allocated to a patient. Table 4.1 describes the actions performed by blood banks and the related data that is available, and indicates which data is included in the records extracted for STEP and subsequently used in this PhD study. Patient specific blood bank transfusion records for the year 2000, from 1st January 2000 to 31st December 2000, inclusive, were extracted from the Scottish National Blood Transfusion Service blood banks that use the Progesa blood bank computer system (SNBTS/Progesa blood bank).

Table 4.1 Hospital blood bank actions: pre-transfusion testing and blood component assignments

Blood bank actions	Patient group	Status in study
Group and screen ▪ Patients' red cell types (Rh and ABO) determined ▪ Patients' plasma tested for clinically significant antibodies to red cell antigens	Transfusion request submitted in advance of planned surgery	Not selected for inclusion in initial data extraction
Crossmatch – As above plus: ▪ Patients' sample tested for compatibility with one or more red cell units ▪ One or more red cell units assigned to patient	Transfusion request submitted when need for blood is anticipated	Selected in initial data extraction
Assignment – As above plus: ▪ One or more of the assigned red cell units is not deassigned and is therefore assumed to be "used"	Transfusion request fulfilled when blood needed	Selected from extracted data for inclusion in study

For the study, records of assigned units were extracted along with relevant patient details from the blood bank computer system. These records were compacted by 24-hour period, using patient identifier number and transfusion event date to facilitate record linkage by date variables at a later stage of dataset development. Compacted transfusion records are referred to as transfusion day records (TDR). Thus the transfusion data available for the study included all transfusion day records that contain units of any blood component (red blood cells, platelets, fresh frozen plasma, and cryoprecipitate) assigned to a patient during the study period.

Transfusion day records contain data for the number of units of blood component that are assigned to individual patients and the number of units that were subsequently deassigned (and so known not to have been transfused). Transfusion day records do not contain a reliable record of the actual infusion of each unit of blood. This has two important consequences for the study. Firstly, an estimate of the actual number of units assumed to be transfused into a patient, referred to as "units used", had to be calculated, and equals the number of units assigned minus the number of units deassigned. A previous validation of this assumption has been carried out by SNBTS by comparing blood bank transfusion records with specific audit data (Palmer, personal communication). Secondly, the date of blood component assignment must be used as a proxy for the date of use of blood units. Transfusion day records that contained data for one or more blood component units used were selected for inclusion in the final study dataset.

Some transfusion day records lacked complete patient identifying information. This can occur when the allocation of patient details is urgent or when full names are for any reason unavailable at the time of blood component issue. In these cases standard operating procedures permit the use of proxy forename and/or surname data in the blood bank transfusion record, for example "unknown/male", "flying/squad", "accident/emergency", "baby/X", together with an emergency blood order number that is allocated by the admitting hospital department. For medical legal reasons the SNBTS policy has been to preserve the identifying data submitted to the blood bank with each transfusion request without subsequent alteration. Therefore, so called "emergency" identifiers are retained in the blood bank computer system with the potential to appear in the transfusion records extracted for the study. Only where appropriate identifying information was available could a unique

patient number be generated by which all records would be identified as belonging to an individual patient: this is termed the patient identifier (PID) (the process is described more fully in section 4.3).

Transfusion day records contain the age and sex of the recipient, the date and hospital of transfusion, and the number of units of each component assigned and deassigned, and are listed in order of unique patient identifier (Table 4.2).

Table 4.2 Data variables in transfusion day records

Variable	Description
Age	Age of patient
Sex	Sex of patient
Event date	Date of transfusion
Hospital	Transfusion event hospital
Red issued	Number of red cell units issued per transfusion record
Red returned	Number of red cell units returned per transfusion record
Platelets issued	Number of adult dose equivalent units of platelets issued per transfusion record
Platelets returned	Number of adult dose equivalent units of platelets returned per transfusion record
FFP issued	Number of fresh frozen plasma units issued per transfusion record
FFP returned	Number of fresh frozen plasma units returned per transfusion record
Cryoprecipitate issued	Number of cryoprecipitate units issued per transfusion record
Cryoprecipitate returned	Number of cryoprecipitate units returned per transfusion record
Age 1 (years)	Age in years at first appearance in study SMR data
Age 1 (months)	Age in months at first appearance in study SMR data

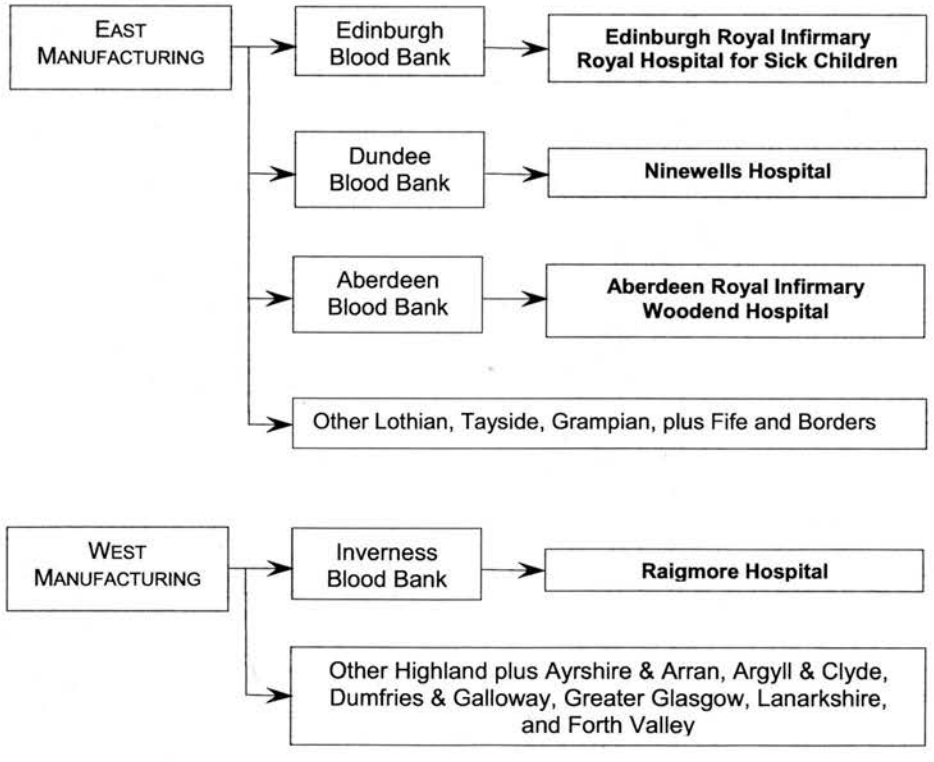
4.2.2. SNBTS delivery data

Data was available for the year 2000 for the total number of units of each blood component supplied by SNBTS to blood banks relevant to the study. A total red blood cell supply figure for all Scotland was also available (Stack, personal communication). This information was used to calculate the proportion of blood component units supplied across all of Scotland that was supplied to hospitals included in the study. Further, the red blood cell supply data

was used in calculations to estimate the standardised age and sex specific rates of blood component use for the study data (Chapter 7).

In order that the study population can be understood in the proper context the SNBTS blood distribution model is outlined here (Figure 4.2). Blood components are delivered by the SNBTS East Manufacturing (EMAN) unit in Edinburgh to hospital blood banks in the east of Scotland: namely Edinburgh, Dundee and Aberdeen. The SNBTS West Manufacturing (WMAN) unit in Glasgow delivers blood components to hospitals in the west of Scotland and also to the Inverness blood bank. The main hospitals served by Edinburgh, Dundee, Aberdeen and Inverness blood banks, and for which data was available for the study, are listed in Figure 4.2 (full details of all hospitals in study are reported in Appendix A.1). The other hospitals in Scotland receive their supply of blood directly from SNTBS, and not via a regional blood bank.

Figure 4.2 SNBTS blood component distribution model for Scotland



* Hospitals in bold are the main hospitals represented by study data (Full explanation for all hospitals: Appendix A.1)

Within the hospital setting blood component units are assigned to an individual patient: blood may subsequently be used by the patient or returned to the blood bank and deassigned. Blood which is not used may be discarded to waste or quality assurance, or distributed to another hospital site. Returned blood may be assigned to a second individual. The transfer of blood components between hospitals may occur when a patient is transferred, along with blood components already assigned to them, to another site or when a special request is made by one site for blood components of a particular or rare type that are held elsewhere. However, SNBTS advice is that the occurrence of transferred units is minimal and does not affect the interpretation of results of blood component use where transfusions can still be linked to the relevant patient's clinical data.

4.2.3. Scottish Morbidity Records

The source of clinical data used in the study was the Information and Statistics Division (ISD) data scheme of Scottish Morbidity Records (SMR), specifically SMR01 records. SMR01 comprises general inpatient and day case data for all acute specialties excluding obstetrics, psychiatry and geriatrics. The data recorded in SMR01 records includes variables for patient characteristics, clinical data and episode management which can be used to build a picture of the patient journey through hospital care (Table 4.3) (described further in SMR coding conventions, below).

Guidelines require the data to be submitted by hospitals to ISD within six weeks of date of discharge (to be reduced to four weeks by the end of 2007). These time frames are not generally met by hospitals but by the time the data was extracted for the study (in 2004) all SMR01 records for the year 2000 had been submitted. SMR01 records have been collected nationally since the 1960s and have been routinely linked using probability matching of patient details by ISD to the Cancer Register (SMR06) and General Register Office for Scotland (GRO) death records since 1981. Linked SMR01/cancer/death (SMR01-CD) records were used in this study. Maternity (SMR02) and neonatal (SMR11) datasets exist in the SMR data scheme but for technical reasons could not be linked to SMR01 at the time the data was extracted for this study.

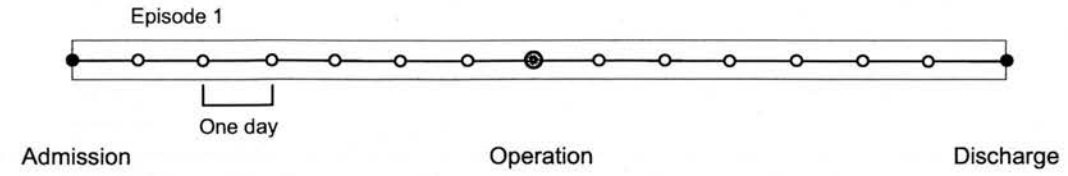
An SMR01 record is generated when a patient is discharged upon the completion of an episode of inpatient or day case care spent under the charge of a consultant within a specific facility and specialty in a hospital setting (a consultant episode). Upon discharge patients may return home (Figure 4.3a) or be transferred to another ward or hospital (Figure 4.3b). Discharge may also follow as a result of the death of the patient (Figure 4.3b). Continuous inpatient stays (CIPS) are specific inpatient admission patterns comprised of more than one contiguous episode during which the patient may be moved between clinicians, wards and specialties, and where a new SMR01 record is generated for each (Figure 4.3c).

Table 4.3 Data variables in linked SMR01/cancer/death records

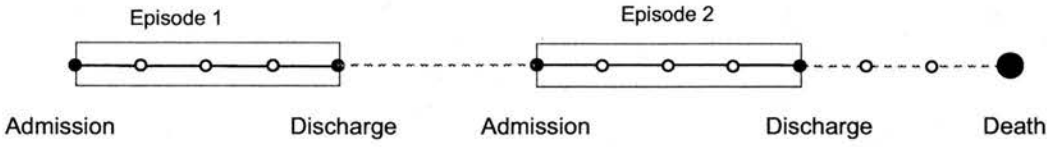
Variable	Description
ISD number	ISD unique patient identifying number
Sex	Sex of patient
Age 2 (years)	Age in years at time of SMR record
Age 2 (months)	Age in months at time of SMR record
Hospital	Hospital of inpatient admission
Date of admission	Date of admission
Date of discharge	Date of discharge
Specialty	Clinician specialty
GMC main	Clinician identification number
Date of operation 1, 2 ...4	Date of operation coded in Op1a, 2a ... 4a
GMC operation 1, 2 ...4	ID number of clinician in charge of operation coded in Op1a, 2a ... 4a
Operation 1a, 2a ...4a	Operation (OPCS-4) coded in Op1a, 2a ... 4a
Operation 1b, 2b ...4b	Operation (OPCS-4) coded in Op1b, 2b ... 4b
Diagnosis	Main diagnosis (ICD-10)
Diagnosis 1, 2 ... 6	Diagnosis (ICD-10) coded in Diag1, 2 ... 6
Discharge type	Type of discharge
Discharge to	Location to which patient is discharged
Date of death	Date of death (General Records Office death record)
Cause	Cause of death (General Records Office death record)
Cancer	Flag of record in cancer register (SMR06)

Figure 4.3 **Representation of examples of different inpatient stay patterns as determined from data recorded in Scottish Morbidity Records**

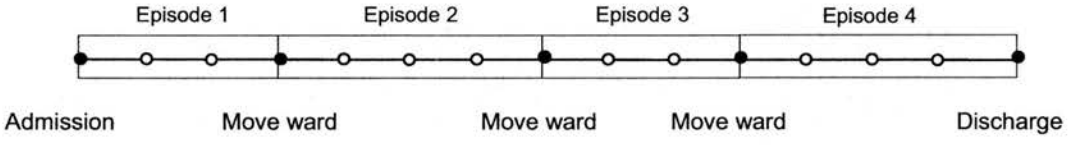
a. Single episodic admission: one SMR01 episode containing an operation



b. Multiple episodic admissions: multiple SMR01 episodes interspersed throughout study period with periods of no inpatient hospital interaction, followed by death



c. Continuous inpatient stay: multiple, contiguous SMR01 episodes of movement between wards before discharge



SMR coding conventions

Following a patient's discharge the clinician responsible for the episode of care writes up a discharge letter. The information in the discharge letter (and sometimes information in the original patient notes) is coded by hospital-based encoders to form a standard information set that is sent to ISD and used to generate SMR records. Guidelines and training manuals for clinical coding are published by the Scottish Clinical Coding Centre (SCCC): these are

based on guidelines from the World Health Organisation but reflect Scottish specific rules which must always be used when coding clinical data in the Scottish context (ISD, online). Surgical operations and procedures are coded using the Office of Population Censuses and Surveys' Classification of Surgical Operations 4th revision (OPCS-4). There are four variables available (Op1a-4a) in each SMR01 for the coding of OPCS-4 data: a primary procedure variable (Op1a) and three others. In addition, there are a further four fields (Op1b-4b) for supplementary OPCS-4 codes that add details such as left or right side of body. The primary procedure and the order in which the other procedures are to be coded should be specified in the discharge letter by the clinician responsible for the episode of care. The clinician should be consulted personally if more than four procedures were carried out during the single episode or where queries regarding the information in the discharge letter arise. In all instances the guidelines require that for OPCS-4 codes the recording of therapeutic procedures takes priority over diagnostic procedures (ISD, online).

Table 4.4 Example of hierarchical coding structure for OPCS-4 codes

Level	Code	Description
Chapter	W	Other bones and joints
Sub-chapter	W37-W92	Joints
Section	W37-W39	Total hip replacement
Sub-section	W37	Primary hip replacement
Specific procedure	W370	Conversion from previous cemented total prosthetic replacement of hip joint
	W371	Primary total prosthetic replacement of hip joint using cement
	W372	Conversion to total prosthetic replacement of hip joint using cement
	W373	Revision of total prosthetic replacement of hip joint using cement
	W378	Other specified total prosthetic replacement of hip joint using cement
	W379	Unspecified total prosthetic replacement of hip joint using cement

Diagnostic data is coded using the International Classification of Diseases and Related Health Problems 10th revision (ICD-10). The International Classification of Diseases is published by the World Health Organization and uses terminology that is internationally accepted. This facilitates comparability in the classification and interpretation of clinical data (WHO, online). SMR01 records contain six variables (Diag1-6) in which ICD-10 codes can be recorded. The first diagnostic variables (Diag1) should contain the ICD-10 code for

the main medical condition that was investigated during the patient's episode of care. If more than one condition is reported in the discharge letter, that which required the most clinical resource input should be recorded; if no specific condition is reported by the clinician then the main symptom or abnormality should be recorded. The remaining diagnostic variables are used to record other existing or developing comorbidities but should not be used to record conditions related to previous episodes of care unless their presence is persistent at the current time (ISD, online).

Table 4.5 Example of hierarchical coding structure for ICD-10 codes

Level	Code	Description
Chapter	II(C00-D48)	Neoplasms
Sub-chapter	C81-C96	Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue
Section	C81	Hodgkin's Disease
Specific diagnosis	C810	Lymphocytic predominance
	C811	Nodular sclerosis
	C812	Mixed cellularity
	C813	Lymphocytic depletion

OPCS-4 and ICD-10 classification systems are organised according to internationally recognised, logical and anatomical hierarchies. The standard format for OPCS-4 and ICD-10 is four character (4-digit) alphanumeric codes: these are hierarchical from left to right, where the first character (letter) defines the broad chapter; the second character (numeral) defines the sub-chapter and so on, with each subsequent character providing more specific and detailed information about the surgical procedure or clinical diagnosis. Examples of the hierarchical coding structures illustrate the large amount of clinical data and the complexity involved in coding (Table 4.4 and 4.5). The specificity and detail of the clinical coding systems employed enable a wide variety of operations and procedures (OPCS-4), and symptoms, abnormalities, injuries and conditions to be recorded (ICD-10).

SMR quality assurance

The completeness of data collection, coding and timeliness of submission to the SMR data scheme is the responsibility of the hospital that is providing the data. The process is overseen by ISD which undertakes rigorous and frequent validation at each stage of data cleaning, storage and publication. When SMR01 records (and other SMR data schemes) are created from submitted information, automatic checks are made by ISD to ensure that recorded procedure and diagnostic codes are valid relative to the respective classification system, record type, date and patient variables, and other codes recorded during the same episode of care (ISD, online; Harley & Jones, 1996).

A report by the Data Quality Assurance team on the quality of SMR01 data is outlined here as evidence of the quality assurance process (ISD, 2004). An assessment of the quality of SMR01 data items recorded by hospitals that represent 95.8% of Scottish NHS acute discharges was begun in the year 2000 and completed in 2002. A 4% sample of three months' data was extracted, of which half just was assessed (5,724 SMR01 records). Data in these records was compared to information recorded in patient case notes and all observed differences were documented. The target at this time was an accuracy of coding of 90% at the 3-digit level: the overall rates of accuracy identified by this audit were 88% for main diagnosis and 91% for main procedure. At the 4-digit level clinical data items were recorded with overall rates of accuracy 81% for main diagnosis and 86% for main procedure. The accuracy rate for coding procedures was affected by the recording of non-operative procedures such as scans, transfusions and injections: excluding these reveals higher accuracy rates of 95% (3-digit) and 89% (4-digit). These rates represent an overall drop in accuracy since the previous audit in 1996/1997, though rates for individual hospitals varied. The report also identified that comorbidity conditions other than the main condition were both misreported and underreported in SMR01 records, and thus the complexity of the patient case mix was portrayed inaccurately. Importantly, the quality assessment included analysis to identify areas where coder accuracy was affected by limited quality of source information versus a lack of access to full medical case notes. The report concludes that routine quality assurance assessments of SMR01 coding accuracy are desirable: routine assessments subsequently began in 2004 (ISD, 2004).

4.3. INFORMATION AND STATISTICS DIVISION PREPARATORY WORK ON SOURCE DATA: PROBABILITY MATCHING & INTERNAL RECORD LINKAGE

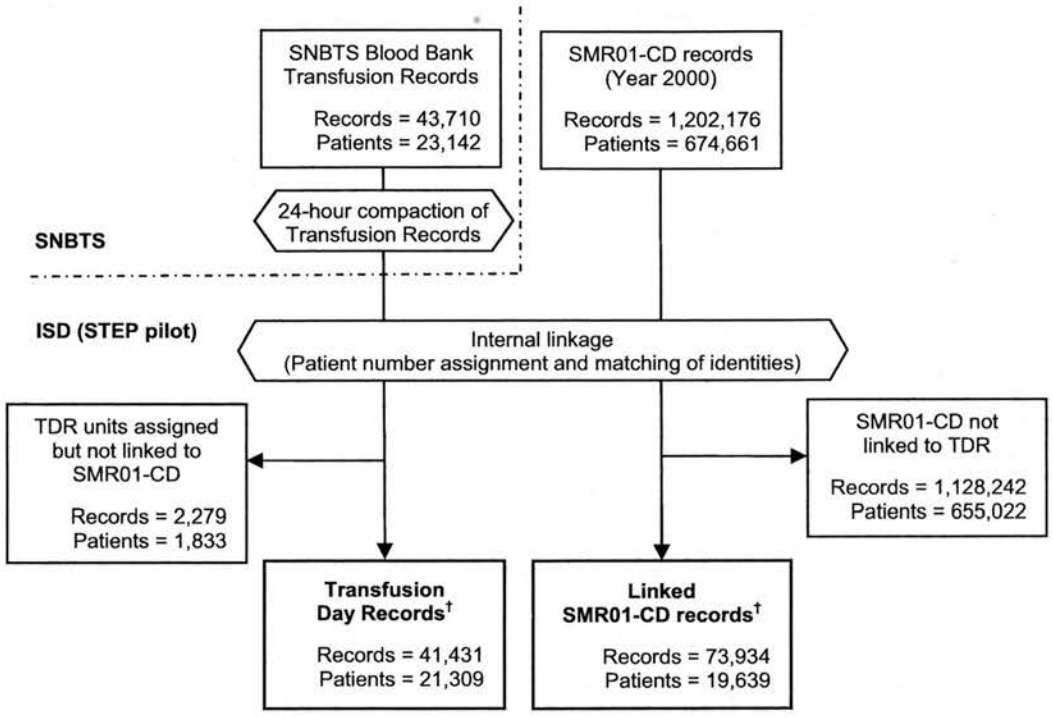
Probability matching is a statistical method developed to address the fact that there may be multiple records for each individual with minor differences in identifiers such as spelling errors, spelling variations or missing data points. The process allocates a unique patient identifier number to all records belonging to an individual patient based on forename, surname and date of birth by considering the available data and accounting for variant or incomplete patient details. ISD employ an algorithm that has been developed so as to perform this function with 98% accuracy (Kendrick & Clarke, 1993; Kendrick, 1997). Transfusion day records with emergency identifiers (described for transfusion records in section 4.2.1) were removed prior to undergoing probability matching by ISD as it would not be possible to identify other records with which these could be appropriately linked and they could not be matched further to SMR01-CD records.

A second record linkage process required for this study was internal record linkage to match patients with transfusion day records with patients with SMR01 records that appear in the Scottish Morbidity Record (SMR) data scheme in the year 2000 in order to select the relevant clinical data for the study population. Some transfusion day records were rejected by ISD at this stage of record linkage because they failed to be linked with a patient identity in the SMR01 data scheme (Figure 4.4).

4.4. TRANSFER OF DATASETS

The source data comprising transfusion day records and SMR01-CD records were provided by ISD as separate SPSS data files with all specific patient identifying information removed and unique patient identifiers attached to all records. Figure 4.4 summarises the steps involved in the data extraction, manipulation, and linkage processes to this point.

Figure 4.4 Record linkages of source data prior to study



† Used as source data to create PhD study dataset

5. METHODS

5.1. INITIAL INVESTIGATION OF SOURCE DATA

The initial investigations carried out on the source data of transfusion day records and linked SMR01/cancer/death records were to examine the data for errors and coding issues and to gain insight into the content and nature of the available data.

The number of blood component units used per patient, and by hospital, for all transfusion day records was checked for erroneous values by eyeballing the available figures. The data was also checked against Scottish National Blood Transfusion Service supply data to make sure that no hospital had a greater number of units used than were originally supplied. The transfusion day records and SMR01-CD records source data were both checked for entry errors in age variables such as minus signs, large values) and the sex variable was checked at the patient level to identify patients with both male and female entries (due, for example, to entry error or sexual reorientation). Descriptive statistics were performed in SPSS (Version 13.0-15.0) to describe the source data.

Transfusion day records were examined at the individual record and the patient level to check data for errors, and to provide summary measures of transfusion such as the number of transfusion records per patient and blood component units assigned, deassigned and used per patient or record, which enabled small or high users of blood to be identified. For patients with multiple transfusion day records the temporal relationship between transfusion events was explored. SMR01-CD records were also examined at an individual record and patient level to gain an understanding of the relationships among procedure codes in variables Op1-4, among diagnostic codes in variables Diag1-6, and between procedures and diagnostic codes (SMR01 coding conventions, section 4.2.2). Coding practices were investigated by examining frequencies of codes recorded in the primary procedures variable Op1 in comparison with all instances coded in variables Op1-4 and similarly for primary diagnoses versus all instances coded in variables Diag1-6.

Relationships between dates of admission, operation and discharge for SMR01 records were also explored and analyses of patient profiles, and in particular of continuous inpatient stay profiles, were attempted. By examining SMR01 records and transfusion day records separately initially and then in relation to each other, a standard approach to describing the patient journey during inpatient hospital care was developed (described further in section 5.2). Understanding gained from the data about patients' clinical and transfusion histories subsequently informed the methods that were employed to relate SMR01-CD records to transfusion day records in order to attribute a clinical reason to transfusion events.

The variables that were in the source transfusion day records and SMR01-CD records have been described in sections 4.2. During the process of initial, exploratory investigations of the data, additional variables were created for both transfusion day records and SMR01-CD records (Table 5.1 and 5.2). Specifically, additional variables were computed for SMR01-CD records to make it easier to understand, manipulate, summarise and report the data given the large amount of clinical information available. The variables relate in the main to the data coded by OPCS-4 codes in operations and procedures variables Op1a-Op4a, and by ICD-10 codes in diagnostic variables Diag1-Diag6 and were the first step in defining red cell using procedures and diagnoses for later stages of the study. Individual OPCS-4 and ICD-10 codes, as well as small clusters of these codes, were used to define the initial red cell using procedures and diagnoses considered for this study (section 5.4). These codes became the basis of the clinical case groups to which blood use was attributed in subsequent analyses (Chapters 6-9).

Table 5.1 Additional data variables generated for Transfusion Day Records

Variable	Description	Computation
Red used	Number of red blood cell units used	RBC assigned minus RBC deassigned
Platelets used	Number of adult dose equivalent platelet units used	PLT assigned minus PLT deassigned
FFP used	Number of plasma units used	FFP assigned minus FFP deassigned
Cryoprecipitate used	Number of cryoprecipitate units used	CRY assigned minus CRY deassigned
Total units	Number of all units used	Total assigned minus total deassigned
Hospital Health Board	Hospital Health Board code	First character of hospital code
Age group	Age group at time of record creation	Age variable grouped by decade

Table 5.2 Additional data variables generated for SMR01-CD records

Variable	Description
Procedure chapter 1 (1 digit) *	1 digit OPCS-4 chapter code for procedure coded in Op1a [A]
Procedure 1, 2, 3, 4 (2 digit) *	2 digit OPCS-4 code of procedure coded in Op1a - 4a [An]
Procedure 1, 2, 3, 4 (3 digit) *	3 digit OPCS-4 code of procedure coded in Op1a - 4a [Ann]
Diagnosis 1, 2, 3, 4, 5, 6 (3 digit) *	3 digit ICD-10 code of diagnosis coded in Diag1 - 6 [Ann]
Blood procedure 1, 2, 3, 4	Procedure in Op1a - 4a if red cell using procedure [Ann]
Main blood procedure	First red cell using procedure in SMR01 record [Ann]
Blood diagnosis 1, 2, 3, 4, 5, 6	Diagnosis in Diag1 - 6 if red cell using diagnosis [Ann]
Main blood diagnosis	First red cell using diagnosis in SMR01 record [Ann]
Supplementary 1, 2, 3, 4	Supplementary procedure in Op1a - 4a [Ann]

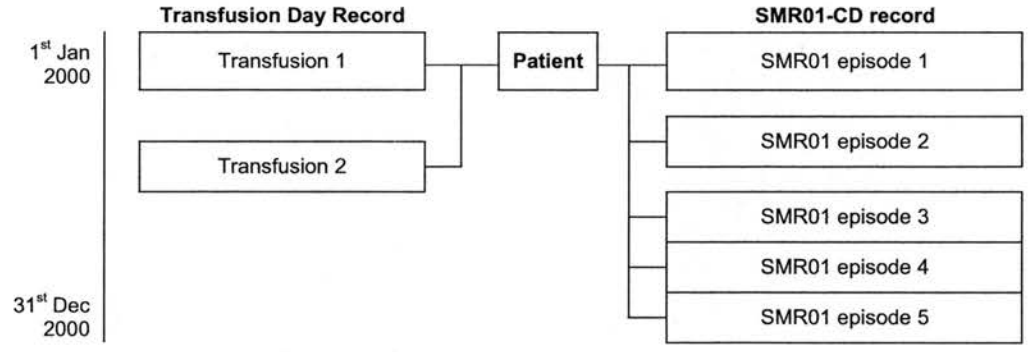
* OPCS-4 procedure and ICD-10 diagnosis codes are 4 digit alphanumeric codes with hierarchical structure. Shortening from the end of the code to 1, 2 or 3 digits reduces the detail of the condition but retains the hierarchical grouping (See materials section). [An]: denotes the alphanumeric code format for procedures or diagnoses, where A=alpha, n=numeric

5.2. DATASET CONSTRUCTION

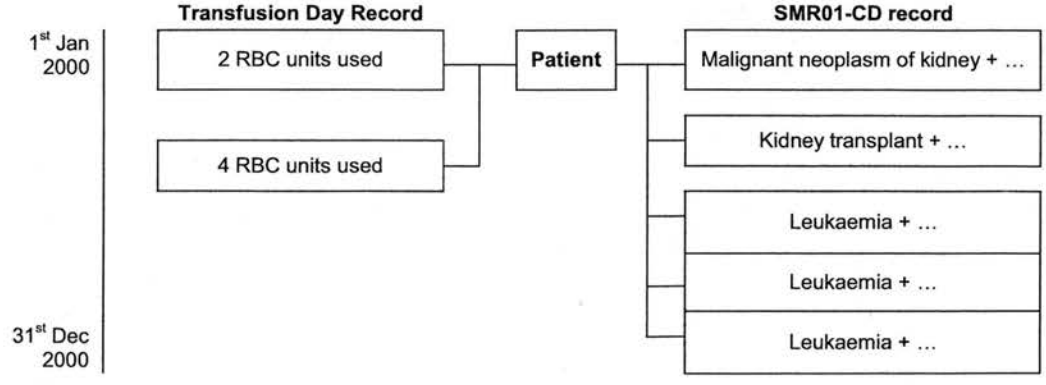
Following from initial investigations of the source data a model was devised to illustrate the relationship between patients' transfusion and clinical data (Figure 5.1). The example illustrated here shows a patient who has two transfusion day records during the year 2000 that can be linked via a patient identifier to five SMR01-CD records comprising multiple episodic admissions and a continuous inpatient stay (CIPS): the CIPS profile is comprised of SMR01 episodes 3, 4 and 5, where the patient enters hospital on the date of admission of episode 3 and leaves on the date of discharge of episode 5. The specific example illustrates a patient transfused with a total of six red blood cell units in the year and who is diagnosed with malignant neoplasm of the kidney, undergoes a kidney transplant and who is subsequently diagnosed with leukaemia.

Figure 5.1 Example overview of a patient's one year transfusion and clinical history

General example:



Specific example:



The model illustrates the potential for patients to have multiple transfusion day records and multiple clinical records thereby instantly generating complexity with regards to the number of potential relationships between records. Viewing the data in this way facilitated understanding of the available data and so the impact of multiple records was identified early in the creation of the study dataset as a large factor in the methodological approaches employed in the study. To fully define all possible relationships between transfusion and clinical each transfusion day record had to be linked with every SMR01-CD records on a patient by patient basis in order that the relevance of the relationships could be assessed. The SPSS restructure function enables a set of records to be restructured so that all records belonging to a patient can be aggregated into a single, complex record. Patient records in this form can subsequently be linked to other datasets via a common variable, in this case the patient identifier number. The decision making process as to which dataset (transfusion or clinical) to restructure involved a series of test examples. By restructuring transfusion day records and linking with original source SMR01-CD records the numbers of blood component units were duplicated: if left unresolved this duplication of data would have posed an inherent complication in all future analyses. Further, because the study aimed to quantify the reasons for blood use, and thereby account for all transfusion day records, it was logical for the transfusion day records to be the key record set to which additional information was linked. Therefore, the restructuring of SMR01-CD records and subsequent merging with relevant transfusion day records was favoured.

Thus, SMR01-CD records were aggregated by patient number and restructured so that all records for each individual patient were combined into a single, complex record that represents the patient's available SMR01-CD information for the year 2000 (Figures 5.2a&b). The unique patient identifier was used to link corresponding SMR01-CD records to transfusion day records for each transfusion recipient. SMR01-CD records could not be linked to a transfusion day record of blood component units used if the patient had no such transfusion day record or if ISD had been unable to assign a patient number to the patient's transfusion day record(s). The majority of SMR01-CD records that could not be linked to a transfusion day record of units used represent the hospital activity of inpatients who were not transfused but who had units assigned and who therefore may be considered to have been at risk of transfusion due to some aspect of the nature of their hospital admission. Unlinked SMR01-CD records were kept separately in case required for future analysis.

Where a patient had more than one transfusion day record the restructured SMR01-CD record was duplicated against each transfusion day record (Figure 5.2c). The resultant file of transfusion day records (units used only) linked to the relevant, available clinical history for the year 2000, that is, the restructured SMR01-CD records, provided a dataset that could be used to consider all potential relationships between blood use and clinical data. Additional variables were computed so that the relationships could be explored further (Table 5.3).

Figure 5.2 **Processes to restructure SMR01-CD records and to merge with transfusion day records to form the study dataset.**

a. Representation of original file formats for source data records: example for two patients

Patient	Transfusion Day Record
A	Transfusion 1
A	Transfusion 2
B	Transfusion 1
B	Transfusion 2
B	Transfusion 3

Patient	SMR01-CD record
A	SMR episode 1
A	SMR episode 2
B	SMR episode 1

b. Restructure SMR01-CD records (transfusion day records not shown)

Patient	SMR01-CD record	SMR01-CD record
A	SMR episode 1	SMR episode 2
B	SMR episode 1	

c. Merge restructured SMR01-CD records with transfusion day records

Patient	Transfusion Day Record	SMR01-CD record	SMR01-CD record
A	Transfusion 1	SMR episode 1	SMR episode 2
A	Transfusion 2	SMR episode 1	SMR episode 2
B	Transfusion 1	SMR episode 1	
B	Transfusion 2	SMR episode 1	
B	Transfusion 3	SMR episode 1	

Table 5.3 Computed data variables for linked study dataset

Variable	Description
Date linked	Date link between SMR01-CD record and transfusion day record
Total date linked	Number of SMR01-CD records date-linked with transfusion day record
Red cell using procedure	Code of red cell using procedure in SMR01-CD record linked to units used
Total red cell using procedures	Number of red cell using procedures related to use of red blood cell units
Red blood cells used (procedure)	Number of red blood cell units attributed to a red cell using procedure

The transfusion day records of units used linked to the restructured SMR01-CD records are herein referred to as the study dataset. The analyses used to describe the source transfusion day records and SMR01-CD records, the linked study dataset, the populations of transfused and non-transfused patients, and subsequent analysis of blood use by clinical case group were carried out using the statistical package SPSS. Thus the next stage was to define the methods with which to attribute clinical case groups to transfusion events. The clinical case groups defined for use in this study and the full methods of attribution are described in the following section (section 5.3).

5.3. ATTRIBUTING A TRANSFUSION EVENT TO A CLINICAL CASE GROUP

This section describes the definition and validation of methods to determine the relationship between data in transfusion day records and data in SMR01-CD records. The aim was to identify all appropriate pieces of clinical data that could be used to infer the reason for transfusion.

The study dataset represents a population of patients that are diverse in terms of the surgical interventions and medical conditions recorded in their clinical records. Using the knowledge gained from approaches adopted by previous studies in combination with essential clinical input specific to this study, separate methods for analysing different patient groups were employed in this study. Therefore a range of clinical case groups considered likely to represent particular populations of transfusion recipients were defined. These formed two main categories: a surgical perspective of procedural events (section 5.3.1) and a diagnostic perspective of chronic pre-malignant and malignant haematological conditions (section 5.3.2).

The rules used to attribute blood use to clinical case group were defined using clinical rationale that addressed the timing of the relationship and identified appropriate clinical information. It is acknowledged that in attributing blood use to case groups by the rules described here, an inference is made about the actual reason for transfusion.

5.3.1. Rule for attributing blood use to surgical procedure case groups

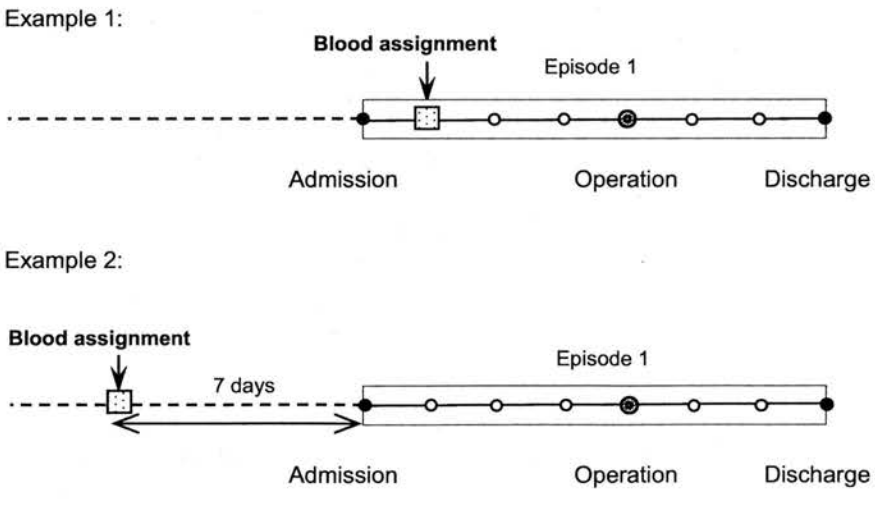
The first case group addressed in the study defined a population of patients who were admitted to hospital for the principal reason of undergoing a major surgical intervention, be that an operation or related procedure for which red blood cell units might be transfused. A description of the rule that was used to attribute blood use to surgical procedures is given here.

Time of blood assignment

The first part of the surgical blood attribution rule defined the temporal relationship between transfusion day records of red blood cell use and SMR01-CD records. Because transfusion day records do not specify the date upon which blood components were used the date of blood component assignment was used as the proxy for date of use. The likely period in which blood assignments would be made in the event of blood being required for surgery was defined as the period from seven days prior to admission to the date of the procedure, thereby including pre-admission blood assignments. This timeframe was subsequently extended to the period from seven days prior to admission to the date of discharge to include pre-admission blood assignments and blood assignments that may be made during the post-operative period. Figure 5.3 illustrates the temporal relationship between the date of blood assignment and admission, operation and discharge dates.

To reiterate, the transfusion day record and SMR01-CD record were related to one another if the date of blood component assignment fell between seven days prior to admission date and the date of discharge.

Figure 5.3 Surgical blood attribution rule: date rule



Red blood cell units are attributed to a red cell using procedure if the date of blood use falls within 7 days prior to admission and date of discharge

Defining the case group by identifying the appropriate red cell using procedure

The second part of the rule addressed the identification of a clinical case group to which the transfusion event could be attributed. Blood use was attributed to the relevant procedural information coded in the OPCS-4 variables of SMR01-CD records that had been identified as satisfying the temporal part of the surgical blood attribution rule. Here the term "procedures" refers to both surgical operations and surgical procedures coded using OPCS-4; "red cell using procedures" herein refers to the specific surgical case groups defined for this study that were expected to be important users of blood (Table 5.4).

Table 5.4 Surgical procedures and OPCS-4 codes defined as red cell using procedures

Red cell using procedure	OPCS-4 code(s)
Operations on tissue of brain	A01-A10
Operations on thyroid or parathyroid glands	B08-B16
Open placement of prosthesis in trachea	E41
Excision of lung	E54
Open extirpation of lesion of lung	E55
Other operations on lung	E59
Open operations on oesophagus	G01-G13
Excision of colon	H04-H11
Excision of rectum	H33
Transplantation of liver	J01
Partial excision of liver	J02
Transplantation of heart	K01-K02
Operations on valves of heart and adjacent structures	K25-K38
Open bypass graft operations (minus revisions & revisions)	K40-K46
Emergency replacement or bypass of aneurysmal segment of aorta	L18, L20
Other operations on aorta	L16, L19, L21-25
Reconstruction of renal artery	L41-L43
Transplantation of kidney	M01
Open operations on prostate	M61-M64
Hysterectomy	Q07-Q08
Open reduction of fracture	W10-W23
Closed reduction of fracture	W24-W26
Total hip replacement (minus revisions & revisions)	W37-W39
Total knee replacement (minus revisions & revisions)	W40-W42
Replacement of head of femur	W46-W47

The red cell using procedures was defined experientially from evidence in the published literature, and in particular using clinical data in Maximum Surgical Blood Order Schedules (MSBOS) (McClelland, personal communication). Maximum Surgical Blood Order Schedules are guidelines for the maximum number of red blood cell units that can be cross-matched pre-operatively for a range of common elective, surgical procedures. Lists of this sort were developed in order to facilitate reductions in the number of red blood cell units cross-matched for surgery and represent potential targets for reducing blood utilisation, and hence major blood using procedures (SIGN, 2001).

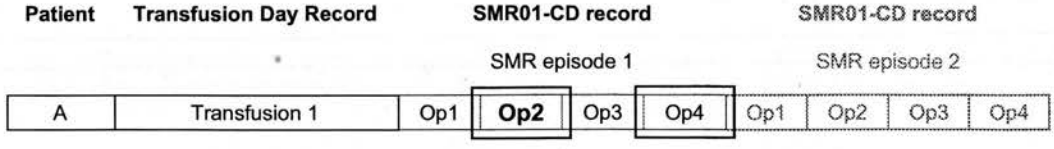
The assumption that the red cell using procedure may be coded in any one of the four available OPCS-4 variables was tested to assess whether multiple red cell using procedures per SMR01-CD might be identified thereby resulting in competition between surgical case groups to which blood could be attributed. An instance where more than one red cell using procedure is coded in a single SMR01-CD record is termed intra-episode competition (Figure 5.4a). Given that Op1-4 are coded with a convention of priority where Op1 is the principal variable intra-episode competition was addressed by accepting the first red cell using procedure encountered in the episode, when reading from variable Op1 to Op4 in order, as the defining red cell using procedure.

An instance where more than one SMR01 record containing (at least) one red cell using procedure can be related to a single transfusion day record according to the surgical blood attribution date rule is termed inter-episode competition (Figure 5.4b). Despite the use of the temporal date rule to determine an appropriate relationship between transfusion day records and SMR01-CD records the issue of inter-episode competition arises where a patient has closely occurring or contiguous inpatient admissions episodes, such as in the case of a continuous inpatient stay. Because the temporal date rule is not confined to linking the date of transfusion to within an episode and instead allows a period of seven days before the date of admission in which a transfusion event may occur, transfusion events may be related to more than one SMR01 record if this window of seven days overlaps with a previous episode. However, if this is the case but the previous episode did not contain a red cell using procedure, then inter-episode competition between red cell using procedures does not arise.

Figure 5.4 SMR01-CD record intra-episode and inter-episode competition

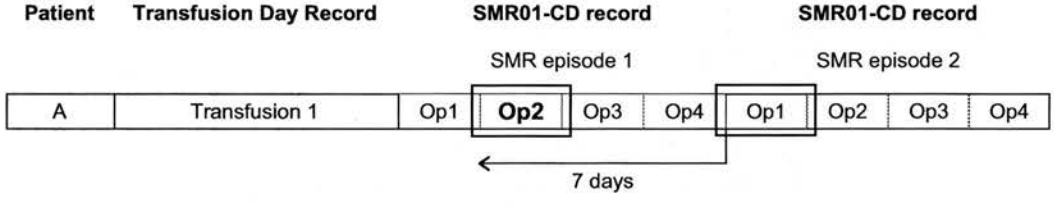
a. Intra-episode competition

Transfusion day record can be linked by date rule with an SMR01-CD record that contains two red cell using procedures (highlighted by boxes). By surgical rule, blood is attributed to Op2 of SMR episode 1.



b. Inter-episode competition

Transfusion day record can be linked by date rule with two SMR01/cancer/ death records that each contains a red cell using procedure (highlighted by boxes). By surgical rule, blood is attributed to Op2 of SMR episode 1.



For the study dataset inter-episode competition for surgical red blood cell use was assessed by calculating the total number of red cell using procedures that could potentially be related to each transfusion day record. Whilst informing the methods at this stage the findings for analyses of inter-episode competition are reported in full in section 8.3 for the sake of clarity and completeness of understanding of results. In summary, the findings suggest that inter-episode competition rarely occurs and so it was not considered to affect the interpretation of blood use by procedural case group. Further, in these scenarios episodes are close together and so the underlying clinical condition in each is likely to be the same anyway: that is, it is considered unlikely in these instances that choosing one red cell procedure over another will affect the type of procedure to which blood is attributed. Inter-episode competition was addressed using the same approach as was used for intra-episode competition: blood was attributed to the first occurring red cell using procedure across Op1-4 variables of the first episode to link by date rule to the transfusion day record is chosen.

To conclude, the steps required to attribute red blood cell use to a red cell using procedure so that red blood cell use by surgical case group can be quantified are summarised in Table 5.5. If an SMR01-CD record could be linked by the surgical blood attribution date rule to a transfusion day record of red blood cell units used and it contained an OPCS-4 code(s) for a red cell using procedure case group then the red blood cell units were attributed to that case group (Table 5.5). If more than one red cell using procedure could be linked to a single transfusion day record of red blood cell use then units were attributed to the first occurring red cell using procedure as described in the explanation for the resolution of intra-episode and inter-episode competition (Figure 5.4).

Table 5.5 Summary of attribution of red blood cell units to clinical case groups according to the surgical blood attribution rule

Clinical case group	RBC units used	Date rule satisfied	Number of potential procedures	RBC units attributed to clinical case group:
Transplantation of kidney	Yes	Yes	1	Transplantation of kidney*
Transplantation of kidney	Yes	No	1	No
Transplantation of kidney	No	Yes	1	No
None	Yes	Yes	0	No
Transplantation of kidney & Excision of bladder	Yes	Yes	2	Transplantation of kidney*

* If Transplantation of kidney is first occurring red cell using procedure in episode or across episodes

5.3.2. Rule for attributing blood use to patients with haematological conditions

The second category of clinical case groups identified for analysis of blood use attributed to clinical reason defined a subset of patients diagnosed with chronic pre-malignant and malignant haematological conditions. The diagnoses included in the study were malignant neoplasms of lymphoid, haematopoietic or related tissue, and of uncertain or unknown behaviour, and the pre-malignant conditions were myelodysplastic syndromes and polycythaemia vera (Table 5.6).

Table 5.6 Diagnoses of malignant and pre-malignant conditions defined as haematological case groups

Clinical case group	ICD-10 code(s)
Lymphoma	C81-C85
Myeloma	C90
Leukaemia	C91-C95
Myelodysplastic syndromes Polycythaemia vera	D45 & D46

Some patients may have had other medical conditions coded in SMR01-CD records but the haematological conditions defined here were considered to be of particular clinical interest and relevance to transfusion practice. The rule for the attribution of blood to haematological case groups made the assumption that a diagnosis of malignant neoplasm of lymphoid or haematopoietic tissue, myelodysplastic syndromes or polycythaemia vera was the underlying cause for any red blood cell transfusion during the whole study period (one year) because of the nature of the conditions and treatment protocols that require multiple transfusions over a protracted period of time. Therefore, if a patient was diagnosed with one of the haematological conditions defined here then all transfusion events during the study period were attributed to the diagnosis (Figure 5.5).

Where a patient is diagnosed with more than one blood using haematological condition during the study period, competition was resolved in the same way as was used for competition between surgical case groups, that is, by attributing blood use to the first such

diagnosis in the patient's SMR01-CD records in the study period. Competition between haematological diagnoses was assessed and the findings reported in full in section 8.3. In summary, few patients were diagnosed with more than one of these conditions and where competition did occur the combinations of diagnoses reflect changes that might be expected in response to the development of symptoms and progression of disease. The attribution of red blood cell use to haematological diagnoses is summarised in Table 5.7.

Figure 5.5 Haematological blood attribution: summary

Clinical rule: Specified haematological disease coded in any episode in study period

Date rule: All transfusion day records during study period

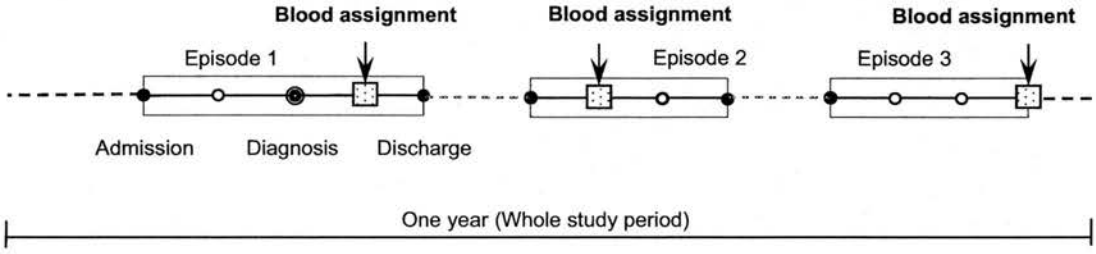


Table 5.7 Summary of attribution of red blood cell units to clinical case group according to the haematological malignancy blood attribution rule

Clinical case group	RBC units used	Number of potential diagnoses	RBC units attributed to clinical case group:
Lymphoma	Yes	1	Lymphoma
Lymphoma	No	1	Lymphoma
None	Yes	0	No
Leukaemia & Lymphoma	Yes	2	Leukaemia*

* If Leukaemia is first occurring procedure in episode or across episodes

5.4. ANALYTICAL FUNCTIONS IN SPSS AND OTHER ANALYTICAL TOOLS

The common processes in the computer software package, SPSS, that were used to investigate the study dataset, include frequencies and descriptive statistics in order to report the mean, standard deviation, range and sum for selected variables. The sum of variables, for example blood component units used by red cell using procedure or number of patients per age group could also be explored using the aggregate function.

Further, the aggregate function was used to analyse data at the patient, rather than record level by aggregating by patient identifier, and by a similar method, at the hospital level and by age group. When aggregating by patient identifier, the first age at time of transfusion, first age group or first sex code from the patient's multiple records was returned in the aggregate as summary variables for subsequent analysis at the patient level. The maximum error incurred in doing so in the case of age was one year (such as if a patient had a transfusion day record at the very start and another at the very end of the year) and was the difference between one age group and the next for age group analysis (such as if patients were in the upper year of the age band and aged further whilst in the study). The effect on the sex variable was expected to be negligible as discrepancies in sex coding are rare. Aggregating data in this way was the best approximation that could be made to analyse data on a patient basis.

Data generated by analytical functions in SPSS was also exported to Microsoft Office Excel (2003) for further analysis.

5.5. OVERVIEW OF METHODS EMPLOYED IN STUDY

The surgical and haematological blood attribution rules and subsequent analyses by clinical case group enabled an inference to be made about a likely reason for transfusion. However, it did not preclude blood component units that could be attributed to surgical and haematological case groups from being attributed to other, alternative or additional clinical case groups. Using the methods described here, transfusion day records were flagged as being related to particular clinical case groups but were effectively still available for attribution to other potential clinical case groups in subsequent analyses. Indeed, as will be seen from the findings reported in section 8.4, some transfusion day records could be linked to both surgical case groups and haematological case groups and the overlap of blood component units between the two was quantified. Therefore, the methods employed to analyse blood use by clinical case group enabled different views of the data to be described simultaneously, and further, allows for the flexibility of making future changes to methods in response to changes in factors that might influence the blood attribution rules.

6. RESULTS: STUDY DATASET

6.1. DESCRIPTIONS OF COMPONENT DATA OF STUDY

6.1.1. Transfusion record data

Blood bank transfusion records of blood component assignments (1st January 2000 to 31st December 2000, inclusive) were extracted from the computer system utilised by SNBTS blood banks and were compacted into 24-hour transfusion day records (section 4.3). Transfusion day records were provided for analysis in a 3.79MB SPSS file. Descriptive statistics of transfusion day records of units assigned and units used are given in Table 6.1. Less than half of patients with transfusion day records were male, the average age was approximately 60 years old and each patient had on average two records. 58.7% of patients with a transfusion day record of blood component assignment had a transfusion day record of blood component use.

Table 6.1 Descriptive statistics for the transfusion day records available for study

Statistic	TDR units assigned	TDR units used
Patients (n)	21,309*	12,514
Transfusion day records (n)	41,431*	27,172
Transfusion day records per patient (range)	1-227	1-227
Transfusion day records per patient (mean, SD)	1.94, 3.23	2.17-3.92
Sex (% Male)	48.6	46.4
Age in years (range)	0.1-101.5	0.1-101.5
Age in years (mean, SD)	59.62, 22.00	64.2, 20.4

* Cross-reference with Figure 4.4 SD: standard deviation

Initial investigations identified two coding issues within transfusion day records: both were easily addressed in the early stages of the study. In one transfusion day record the age in years at time of transfusion was recorded as a negative number, -0.1. This may have been the result of an entry error in the decade of birth (meaning that the patient was actually 99.9 years old), or could simply have meant that the patient was 0.1 years old. This patient was transfused with just one blood component unit of fresh frozen plasma. Further, the transfusion day record could not be linked to an SMR01-CD record which may have been because the patient had a different type of SMR record, for example, maternity and neonatal (SMR02 and SMR11) data for which was not available for the study at the time of data extraction. Together these facts suggested that the patient was a neonate. The age was subsequently corrected to 0.1 years.

Secondly, calculating the number of units used (equal to units assigned minus deassigned) for the blood component cryoprecipitate resulted in negative values. It was evident that for all transfusion day records the number of units of cryoprecipitate assigned had been incorrectly labelled as deassigned and vice versa. The original variable names were not changed but the calculation for units of cryoprecipitate used was altered to units deassigned minus assigned thereby giving positive values for cryoprecipitate use. There were no obvious anomalies such as extremely large numbers in the number of blood component units recorded for the assigned or deassigned, and consequently used blood component variables at both a record and patient level. Table 6.2 reports the number of units assigned and the number of units used for each blood component. Approximately half of the red blood cell units assigned are assumed to have been transfused, whereas approximately 95% of all other blood component units assigned are assumed to have been transfused.

Table 6.2 **Blood component units assigned and used: transfusion day records linked to at least one SMR01-CD record**

Blood component	Units assigned (n=135,607)	Units used (% of assigned) (n=76,130)
Red blood cells	118,727	60,130 (50.6)
Platelets	5,051	4,795 (94.9)
Fresh frozen plasma	9,983	9,446 (94.6)
Cryoprecipitate	1,846	1,759 (95.3)

6.1.2. SNBTS supply data

Using the Scottish National Blood Transfusion Service (SNBTS) supply data it was calculated that a total of 86,369 red blood cell units were supplied to SNBTS/Progesa blood banks that were representative of the study data (Table 6.3). Therefore, the study transfusion data relates to blood component use for hospitals in Eastern regions of Scotland (total 60,130 red blood cell units used) which represents approximately 38% of the 225,422 red blood cell units supplied by SNBTS to the whole of Scotland in the year 2000. The assumption applied in this study is that red blood cell supply and use is uniform across all of Scotland and therefore, for the purposes of predicting red blood cell use for the whole of Scotland, the study data represents 38% of the Scottish population. Therefore, the estimated number of red blood cell units used in the whole of Scotland in 2000 is 158,863, which equates to the use of 70% of the red blood cell units supplied: this is comparable with the use of 62.0% to 77.7% of the red blood cell units supplied to the blood banks included in the study (Table 6.3).

The number of red blood cell units *supplied* per 1,000 head of population for the study population was 44.9. The number of red blood cell units *used* per 1,000 head of population for the study population was 56.4 overall; 66.4 red blood cell units used per 1,000 head of population for males and 49.6 red blood cell units used per 1,000 head of population for females.

Table 6.3 **Context of study dataset: SNBTS supply data and study dataset blood use data**

Area	RBC units supplied	RBC units used	RBC units used/ supplied
Inverness blood bank	8,827	5,635	63.8%
Aberdeen blood bank	23,724	18,443	77.7%
Dundee blood bank	21,857	13,560	62.0%
Edinburgh blood bank	31,961	22,443	70.2%
Sub-total study	**86,369**	**60,081***	**69.6%**
Sub-total non-study†	139,053		
Total all Scotland	**225,422**		

† Calculated from total RBC units supplied to all Scotland minus total supplied to blood banks included in study. * 60,130 RBC units in study dataset in total: 49 RBC units for non-SNBTS/Progesa hospitals not reported in Table 6.3.

6.1.3. Scottish Morbidity Record data

Two files of SMR01 records and related cancer and death records were available for study. One was a large SPSS file (213MB) of all year 2000 SMR01-CD records for the whole Scottish population; the second was an SPSS file (14.8MB) of all SMR01-CD records for the year 2000 that had undergone internal record linkage and could be linked to patient identities in the file of transfusion day records of unit assignments. Descriptive statistics for the two SMR01-CD datasets are given in Table 6.4. Patients with SMR01-CD records and who could be linked to transfusion day records of units assigned had on average more than twice as many SMR01-CD records per patient, included a higher proportion of males, and were on average seven years older than inpatients who could not be linked to transfusion day records of units assigned.

As with transfusion day records, minor irregularities in coding were identified within the linked SMR01-CD records. Three patients had a mixed sex coding: all were initially coded as male and were coded in subsequent SMR01-CD records as female. The recorded sex was not adjusted for this study as it was not considered to have a bearing on interpretation of data at the individual record level, and, when data was aggregated to the patient level, the first sex code per patient was always selected (that is, upon aggregation the patients with anomalous sex entries were all considered to be male).

Table 6.4 Descriptive statistics for SMR01-CD record data

Statistic	All Scotland SMR01-CD‡	Linked† SMR01-CD
Patients	674,661	19,639*
SMR01-CD	1,202,176	73,934*
SMR01-CD per patient (range)	1-142	1-123
SMR01-CD per patient (mean, SD)	1.78, 2.07	3.76, 4.22
Sex (% Male)	48.1	51.1
Age in years (range)	0-111	0-101
Age in years (mean, SD)	53.42, 23.54	60.74, 20.56

‡ SMR01-CD: SMR01/cancer/death records. † Linked to patient identities with transfusion day records of assigned blood component units. * Cross-reference with Figure 4.4.

Multiple SMR01-CD records per patient and the large amount of clinical data recorded in each SMR01-CD record were identified as likely to cause data handling issues. Intra- and inter-episode competition has been described previously (Figure 5.4). In order to understand the extent of intra-episode competition, the relative importance of each red cell using procedure and blood using diagnosis code to others in the same SMR01 record was determined by exploring the frequency of coding across the multiple procedure and diagnosis variables in relation to the number coded in the relevant primary variable. All red cell using procedures defined in this study, with the exception of transplantation of heart (which includes transplantation of heart and lung), were coded in the primary OPCS-4 procedure variable, Op1, more than 50% of the time, and 17 of those 28 red cell using procedures were coded in Op1 more than 90% of the time (Table 6.5). Transplantation of heart and lung (K01) and transplantation of heart (K02) were not coded in any OPCS-4 field in any SMR01-CD record in the source data: this procedure does not appear in the findings of any further analyses. The four malignant or pre-malignant haematological conditions (lymphoma, myeloma, leukaemia, and polycythaemia and myelodysplastic syndromes) were coded in the primary ICD-10 diagnosis variable, Diag1, between 75% and 92% of the time (Table 6.6).

Table 6.5 Coding of red cell using procedures: number of times coded in primary procedure variable compared with all instances in Op1-4

Red cell using procedure	Number of times coded in variable:				
	Op1	Op2	Op3	Op4	Op1/Total
Open placement of prosthesis in trachea	4	0	0	0	100.0%
Total knee replacement (minus revisions)	508	2	2	0	99.2%
Total hip replacement (minus revisions)	1,294	10	3	2	98.9%
Transplantation of kidney	63	2	0	0	96.9%
Replacement of head of femur	445	13	4	1	96.1%
Total hip replacement revisions	213	6	2	2	95.5%
Transplantation of liver	42	1	1	0	95.5%
Excision of lung	192	8	1	1	95.0%
Open operations on prostate	38	0	1	1	95.0%
Total knee replacement revisions	54	2	1	0	94.7%
Open bypass graft operations revisions	16	1	0	0	94.1%
Emergency replacement or bypass of aneurysmal segment aorta	94	2	3	1	94.0%
Hysterectomy	392	17	8	1	93.8%
Excision of colon	610	36	8	1	93.1%
Other open operations on kidney	158	9	2	1	92.9%
Operations on valves of heart and adjacent structures	322	18	6	1	92.8%
Excision of rectum	358	23	8	2	91.6%
Closed reduction of fracture	582	57	12	10	88.0%
Operations on thyroid or parathyroid glands	45	7	0	1	84.9%
Other operations on aorta	193	30	6	0	84.3%
Open extirpation of lesion of lung	14	2	1	0	82.4%
Open reduction fracture	671	120	26	0	82.1%
Open operations on oesophagus	117	22	4	3	80.1%
Other operations on lung	87	16	7	1	78.4%
Partial excision of liver	66	17	4	1	75.0%
Operations on tissue of brain	157	40	15	13	69.8%
Reconstruction of renal artery	31	9	5	1	67.4%
Open bypass graft operations (minus revisions)	1,183	897	178	21	51.9%
Transplantation of heart (includes heart and lung)	0	0	0	0	n/a

Table 6.6 Coding of red cell using haematological diagnoses: number of times coded in primary diagnosis variable compared with all instances in Diag1-6

Haematological diagnosis	Number of times coded in variable:						
	Diag1	Diag2	Diag3	Diag4	Diag5	Diag6	Diag1/Total
Lymphoma	1,938	102	57	9	5	2	91.7%
Myeloma	943	50	37	10	4	2	90.2%
Leukaemia	2,375	252	76	15	12	2	86.9%
Polycythaemia & myelodysplastic syndromes	548	82	61	17	14	5	75.4%

Anomalous coding of transplantation of heart and lung and transplantation of heart

Because transplantation of heart, and heart and lung, were not coded in any SMR01-CD record in the study dataset the coding for these procedures was checked for the whole of Scotland in the year 2000. Data available for all SMR01-CD records for the whole of Scotland in the year 2000 contained records coded with one heart and lung transplant (K01) and five heart transplants (K02), all of which are found in the primary OPCS-4 variable, Op1. However, upon further investigation the heart and lung transplant and three of the heart transplants appear to have been coded erroneously. The heart and lung patient had one SMR01 record in the year 2000 for an admission to a Glasgow hospital in which they entered hospital one day and were discharged the next, an unexpected period of admission considering the coding of allotransplantation of heart (K011) in the primary procedure field. Further, no other procedures were coded in the remaining OPCS-4 variables. The admission profile bore more relevance to the unrelated and unexpected diagnosis coded in the primary ICD-10 variable: K011, impacted teeth. Therefore it is assumed that the diagnostic code K011 was erroneously recorded in the procedure variable where it takes on a completely different meaning. A summary of the SMR01 records in which transplantation of heart is coded in Op1 is given in Table 6.7. By looking at the diagnoses recorded for these patients it was possible to identify where the apparent K02 code had been correctly entered against patients given that in two cases the diagnoses were for heart related conditions and their inpatient patterns consisted of multiple admissions. Two erroneous cases were patients at dental hospitals with single day admissions who also had diagnosis codes for dental caries, which,

if coded in the procedure variable are mistaken for heart transplants. In a third case a double coding error had occurred: because the admission was again at a dental hospital it is presumed that the K02 coding in the procedure variable ought to have been coded in the diagnosis variable to indicate dental caries. However, the actual code that was entered in the diagnosis variable is also presumed to be incorrect given that the patient is an eight year old for whom a delirious mental state due alcohol withdrawal is unexpected.

Table 6.7 SMR01 coding for transplantation of the heart and transplantation of heart and lung

Hospital	Number of SMR01	Diagnosis (code & description)		Coding summary
Royal Infirmary	18	I259	Chronic ischaemic heart disease, unspecified	Correct coding in Op1
Royal Infirmary	17	I420	Dilated cardiomyopathy	Correct coding in Op1
Dental Hospital	1	K029	Dental caries	Diag1 wrongly coded in Op1
Dental Hospital	1	K029	Dental caries	Diag1 wrongly coded in Op1
Dental Hospital	1	F104	Mental & behavioural disturbance due alcohol: withdrawal state with delirium	Diag1wrongly coded in Op1 plus erroneous Diag1

Op1: Primary OPCS-4 (procedure) variable; Diag1: Primary ICD-10 (diagnosis) variable

6.2. DESCRIPTION OF STUDY DATASET

6.2.1. Records included in study dataset

This section describes the study dataset that was created by linking transfusion day records of units assigned and SMR01-CD records (section 5.2). 41,431 transfusion day records of blood component assignments and 73,934 SMR01-CD records were linked and then the dataset was reduced to transfusion day records of units used. Table 6.8 reports the descriptive statistics for the study dataset which are therefore based on transfusion day records of blood component units used. The final study dataset contains the transfusion and clinical data for 11,994 patients (Figure 6.1). Overall, 96.8% of all blood component units used that were recorded in the source data of transfusion day records could be linked to at least one SMR01-CD record in the study dataset. 70.9% of the SMR01-CD records in the source data were included in the final, study dataset.

Figure 6.1 Number of records and patients at stages of study dataset creation

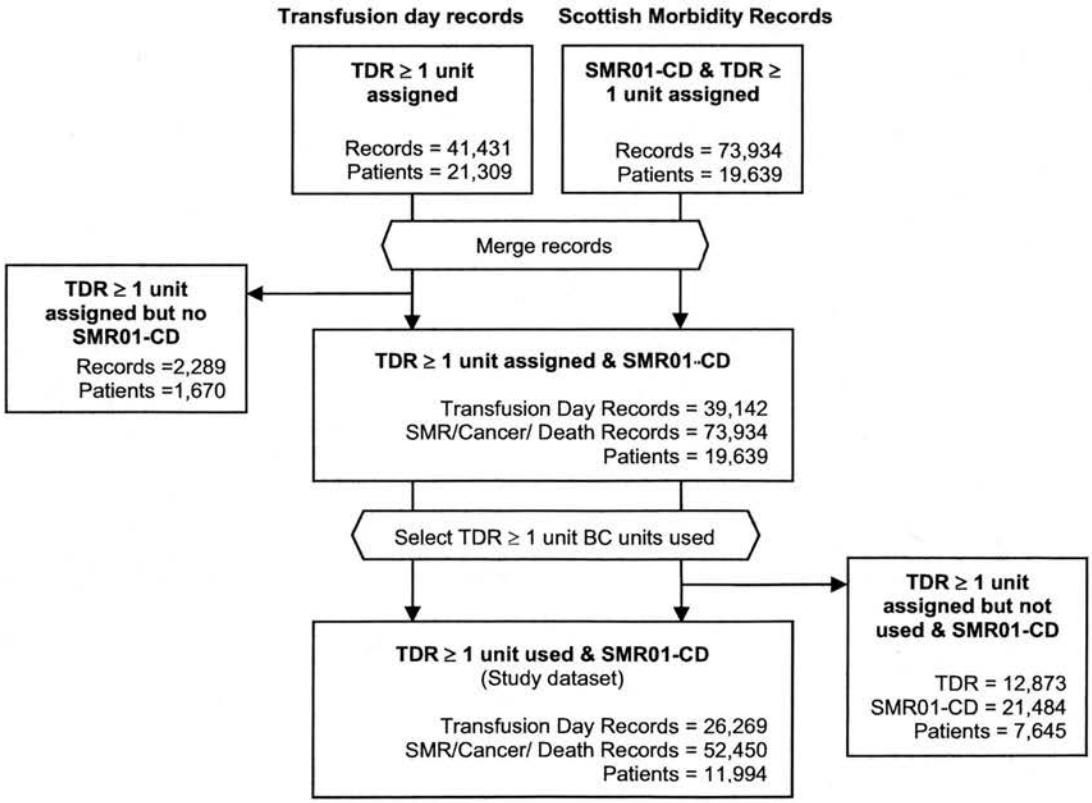
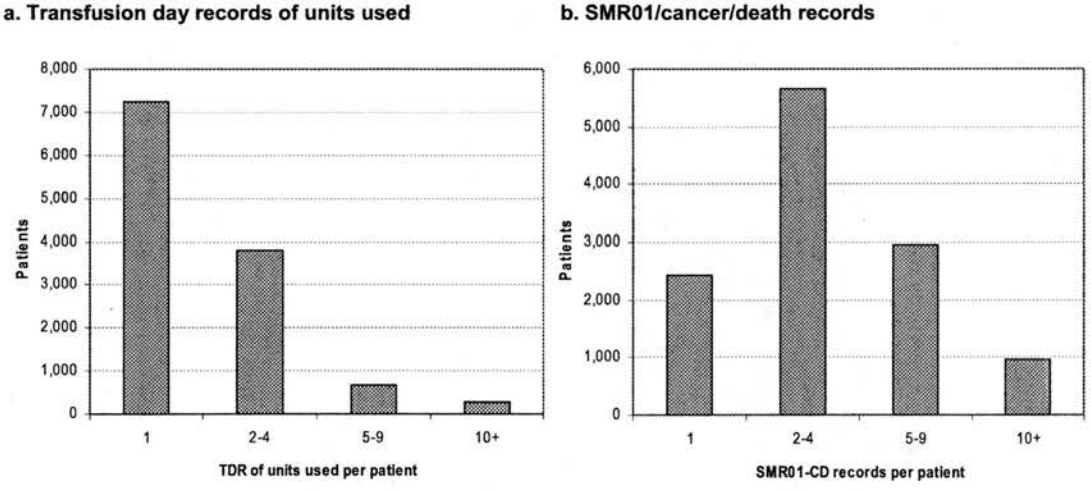


Table 6.8 Descriptive statistics for the study dataset

Statistic	Study dataset
Patients	11,994
Transfusion day records	26,269
SMR01-CD records	52,450
Transfusion day records per patient (range)	1-227
SMR01-CD per patient (range)	1-123
Sex* (% male)	51.4
Age* in years (range)	0-101.4
Age in years (mean, SD)	61.5, 21.3

* Statistics for sex and age from Transfusion day records

Figure 6.2 Records per patient in the study dataset



The number of transfusion day records of units used and SMR01-CD records per patient are described in Table 6.8 and Figures 6.2a and 6.2b. Most patients in the study dataset have one transfusion day record of units used and the average is 2.19 (SD 3.97) transfusion day records of units used. For SMR01-CD records, most patients have two to four and the average is 4.37 (SD 4.75) SMR01-CD records in the study year. The use of blood component units by age, gender and intensity of transfusion are described, for each blood component separately, in Chapter 7.

6.2.2. Records not included in study dataset

Here, the populations of patients with transfusion or clinical records that could not be linked, and therefore do not appear in the study dataset, are described: first, patients with SMR01-CD records but no transfusion day records of blood component units used, and second, patients with transfusion day records of blood component units used but no SMR01-CD records.

The non-transfused patients were those who had at least one SMR01-CD record in the year 2000 but who could not be linked to a transfusion day record. The statistics that describe the non-transfused subgroup are given (Table 6.9). In the year 2000, 1,128,242 SMR01-CD records represented 655,022 patients who had at least one inpatient hospital stay as recorded in SMR01 during that year but who did not have a transfusion day record of any blood component units assigned during that year. 21,484 SMR01-CD represented 7,645 patients who had 12,873 transfusion day records of a blood component unit assigned but who could not be linked to a transfusion day record of units used (Table 6.9). SMR01-CD records that could be linked to transfusion day records of unit assignments but not use represent patients who were at risk of being transfused (by virtue of blood request and assignment being made) but the decision was made not to transfuse. On average, these patients had more inpatient admissions, fewer were male and the average age was older in comparison with patients with transfusion day records of unit assignments.

A small number of patients who had transfusion day records of blood component use but who could not be linked to an SMR01-CD record in the year 2000 are described in Table 6.10. The blood may have been given as an out patient transfusion or the patients may have had an inpatient record for an admission type not included in the SMR01 data scheme. For example, if patients' hospital interaction was coded in maternity or neonatal records (SMR02 and SMR11) instead of inpatient records (SMR01), then the clinical data was not available because these other data schemes could not be linked at the time that the data was extracted for this study. If this explanation is true for some of the unlinked records, then a young population with a high percentage of females would be expected, a hypothesis which indeed the data supports (average age, 44.4 years; 67.4% female) (Table 6.10).

Table 6.9 Patients with SMR01-CD records but not transfused

Statistic	No units assigned	Units assigned but not used
Patients	655,022	7,645
SMR01-CD records	1,128,242	21,484
SMR01-CD records per patient (range)	1-142	1-199
SMR01-CD records per patient (mean, SD)	1.72, 1.94	2.81, 2.99
Sex (% Male)	52.1	48.2
Age in years (range)	0-111	0-100
Age in years (mean, SD)	52.94, 23.64	57.79, 20.52

Table 6.10 Transfusion recipients not linked to SMR01-CD records in year 2000

Statistic	No SMR01-CD record in year 2000
Patients	520
Transfusion day records*	903
Transfusion day records* per patient (range)	1-27
Transfusion day records* per patient (mean, SD)	1.74, 2.55
Sex (% Male)	32.6
Age in years (range)	0.1-101.5
Age in years (mean, SD)	44.43, 29.55
Units used (% of total in originally extracted TDR):	
Red blood cells	2,188 (3.5)
Platelets	115 (2.3)
Fresh frozen plasma	143 (1.5)
Cryoprecipitate	39 (2.2)

* Transfusion day records of units used

6.3. OVERVIEW OF STUDY DATASET

The aim of the study was to create a dataset that could be used for subsequent analysis of blood component use. The results reported in this chapter demonstrate that it is possible to link data from routine sources to create a study dataset that contains both transfusion and clinical data and that the data can be used to describe the patients included in the study, who received blood and had an inpatient admission in the year 2000. The final, linked study dataset (section 6.2) and the patients defined by records that could not be linked (section 6.3) were described here. Further objectives of the study were to use the study dataset to describe blood component use by age, gender and intensity of transfusion (Chapter 7) and to describe the use of blood components by clinical case group, specifically for surgical procedures and haematological conditions (Chapters 8 and 9).

7. RESULTS: TRANSFUSION DATA

7.1. INTRODUCTION TO BLOOD COMPONENT TRANSFUSION

In Chapters 6 it was shown that it was possible to link transfusion and clinical records from routine sources to create a study dataset for blood use analysis. In this chapter, blood component use by age, gender and intensity of transfusion of blood component recipients is described for the transfusion day records of used units that were included in the study dataset (69.5% of RBC units used in the original, extracted transfusion day records). Findings are reported separately for each blood component (sections 7.2-7.5).

Table 7.1 Any use of blood: patient, transfusion day record and blood use data

Statistic	RBC units used	PLT units used	FFP units used	CRYO units used
Patients	11,567	1,422	1,266	253
Transfusion day records	22,471	4,084	2,171	328
Transfusion day records per patient (range)	1-53	1-92	1-223	1-7
Transfusion day records per patient (mean, SD)	1.9, 2.3	2.9, 5.6	1.7, 6.4	1.3, 0.8
Transfusion day records per patient (mode)	1	1	1	1
Sex by transfusion day record (% male)	50.3	57.0	62.8	61.6
Sex by patient (% male)	47.1	62.4	61.0	61.3
Age in years (range)	0-101.4	0-97.3	0-97.7	0-95.1
Age in years per transfusion day record (mean, SD)	63.0, 21.0	51.9, 21.8	57.2, 18.3	52.5, 22.5
Age in years per patient (mean, SD)	65.2, 19.6	57.4, 21.0	60.2, 19.4	52.9, 22.6
Units used *	60,130	4,795	9,446	1,759
Units used per transfusion day record (range)	1-72	1-8	1-34	1-40
Units used per transfusion day record (mean, SD)	2.6, 2.1	1.2, 0.5	4.4, 3.4	5.4, 5.7
Units used per transfusion day record (mode)	2	1	3	1
Units used per patient (range)	1-144	1-93	1-1,776	1-95
Units used per patient (mean, SD)	5.2, 6.9	3.4, 6.3	7.5, 51.6	7.0, 10.3
Units used per patient (mode)	2	1	3	1
Age group transfused with max units used per patient per age group (years)	10-39	30-39	40-49	20-29
Units used per patient per age group (max)	6.7	5.7	20.3	13.9

* Units used refers to the units of the relevant blood component reported by column of table: patients with transfusion day records of RBC units used, the figure reported for units used is the number of RBC units used.

First, in this section measures of transfusion day records and blood use for patients of different subgroups are described. The findings for any use of blood components are described: for example, for red blood cells, any transfusion day record of at least one unit of red blood cells used either alone or in any combination with other blood component types (Table 7.1). The findings for the use of individual blood components are also described: for example, for red blood cells, any transfusion day record of red blood cell use only and no platelet, FFP or cryoprecipitate units used (Table 7.2). 86% of patients who receive red blood cell units during the year receive only red blood cell units, whereas 16% of platelet recipients, 12% of FFP recipients and just 1% of cryoprecipitate recipients were transfused with solely those respective blood component types. The age and sex distributions for each blood component type are approximately the same for patients who received any transfusion compared to patients who received one blood component type only, except for cryoprecipitate, where far fewer males received cryoprecipitate alone (33.3%) than received any cryoprecipitate transfusion (61.3%).

Table 7.2 Single blood component use only: patient, transfusion day record and blood use data

Statistic	RBC units used only	PLT units used only	FFP units used only	CRYO units used only
Patients (% only/any*)	10,003 (86)	224 (16)	155 (12)	3 (1)
Transfusion day records	16,915	586	194	3
Transfusion day records per patient (range)	1-33	1-56	1-18	1
Transfusion day records per patient (mean, SD)	1.69, 1.67	2.62, 5.27	1.25, 1.42	1.00, 0
Transfusion day records per patient (mode)	1	1	1	1
Sex by patient (% male)	44.9	60.3	62.6	33.3
Age in years per patient (range)	0-101.4	0-93.1	0-88.8	35.0-76.9
Age in years per patient (mean, SD)	66.3, 19.2	58.0, 21.4	66.2, 18.0	55.0, 21.0
Units used	41,115	656	666	21
Units used per patient (range)	1-91	1-56	1-145	1-10
Units used per patient (mean, SD)	4.11, 4.46	2.92, 5.44	4.30, 12.0	7.0, 5.20
Units used per patient (mode)	2	1	2	10

Blood component (BC) use aggregated by patient ID and then selected if:
RBC only=RBC>0 & (PLT=0 & FFP=0 & CRYO=0)
PLT only=PLT>0 & (RBC=0 & FFP=0 & CRYO=0)
FFP only=FFP>0 & (RBC=0 & PLT=0 & CRYO=0)
CRYO only=CRYO>0 & (RBC=0 & PLT=0 & FFP=0)

* Percentage of patients transfused with blood component who were transfused only with that blood component type: for example 86% of patients transfused with red blood cell units (n=11,567) were transfused with only red blood cell units and received no other blood component type (n=10,003).

Table 7.3 Combinations of blood component use: patient, transfusion day record and blood use data

Statistic	RBC only*	RBC + other BC	Other BC only	Any**
Patients	10,003	1,564	427	11,994
Transfusion day records	16,915	8,500	854	26,269
TDR per patient (range)	1-33	1-227	1-56	1-227
TDR per patient (mean, SD)	1.69, 1.67	5.43, 9.31	2.00, 3.99	2.19, 3.97
TDR per patient (mode)	1	2	1	1
Sex (% male by patient)	44.9	60.9	61.1	47.6
Age in years (range)	0-101.4	0-97.7	0-93.1	0-101.4
Age in years (mean, SD by patient)	66.3, 19.2	58.1, 23.0	60.8, 20.9	65.0, 19.7
Units used*	41,115	33,357	1,658	76,130
Units used per patient (range)	1-91	2-1,899	1-1,484	1-1,899
Units used per patient (mean, SD)	4.11, 4.46	21.3, 53.0	3.88, 9.15	6.35, 20.5
Units used per patient (mode)	2	6	1	2

Blood component (BC) use aggregated by patient ID and then selected if:
RBC + other BC=RBC>0 & (PLT>0 or FFP>0 or CRYO>0)
RBC only=RBC>0 & (PLT=0 & FFP=0 & CRYO=0)
Other BC only=RBC=0 & (PLT>0 or FFP>0 or CRYO>0)
Any=RBC>0 or PLT>0 or FFP>0 or CRYO>0

* Cross reference Table 7.2. ** Cross reference Table 6.8 for total study dataset data: Table 6.8 reports age and sex per TDR, Table 7.3 age and sex per Patient. Units used = all relevant blood component units by combination of BC reported in column of table. BC: Blood component.

Further, the use of different combinations of blood component types that are clinically meaningful are reported: red blood cell use alone, red blood cell and other components combined, and any combination of other blood components excluding red blood cells (platelet, FFP and cryoprecipitate); subgroups that together total all transfusion day records in the study dataset (final column)(Table 7.3). It is helpful to consider blood component use in this way such as for analysis of donor exposure (section 10.6) or particular resource planning contexts.

In the following sections the findings that are reported for analyses of blood component use by age, gender and intensity relate to all blood component transfusions (sections 7.2-7.5). The age distributions for blood component use are described and the estimated total blood use for Scotland is reported by age and gender for each blood component. The age and gender specific rates of transfusion for each blood component were obtained from the study

data and were applied to the population age structure for Scotland in the year 2000. The calculation had to account for the proportion of the population that was transfused, based on the approximation that the study dataset represents 38% of the red blood cell units supplied by SNBTS to the whole of Scotland in the year 2000, and hence the study dataset represents approximately 38% of the Scottish population, if transfusion practice is presumed to be uniform throughout the country (SNBTS blood supply data; Table 6.3).

The term "intensity of transfusion" is defined for this study as the number of blood component units used per patient during the study, which equates to the number of blood component units used per patient per year as the study period is one year. The findings for intensity of transfusion for each blood component are reported in full presently but briefly the data demonstrates that many patients are transfused at a low intensity and the total units accounted for is small, and conversely, few people are transfused intensively accounting for a large proportion of the units used.

7.2. RED BLOOD CELL USE

The study dataset contained 22,471 transfusion day records of at least one red blood cell unit used, that represented 11,567 patients (red cell recipients) and 60,130 used units of red blood cells (Table 7.4 and Figures 7.1a-c). 50.3% of these red cell recipients were males who accounted for 52.2% of red blood cell units used. On average red cell recipients had 1.9 transfusion day records of red blood cell units used and the mean number of red blood cell units used per patient during the year was 5.2. Red cell recipients also used 1,636 units of platelets, 4,392 units of fresh frozen plasma and 1,182 units of cryoprecipitate. The mean number of all blood component types used per red cell recipient was 6.0 units

20,763 (92.4%) transfusion day records of at least one red blood cell unit used contained no other blood component units used, that is, 10,003 (86.4%) patients transfused with red blood cells only received red blood cells. The findings of descriptive analyses for the population transfused with red blood cells only was summarised previously in Table 7.2 and 7.3.

Table 7.4 Population transfused with red blood cell by age group.

Age group Years	TDR (%) n=22,471	Patients (%) n=11,567	TDR / Patient	RBC units (%) n=60,130	RBC units/ Patient *
0-9	937 (4.2)	303 (2.6)	3.1	1,482 (2.5)	4.9
10-19	469 (2.1)	190 (1.6)	2.5	1,275 (2.1)	6.7
20-29	570 (2.5)	283 (2.4)	2.1	1,896 (3.2)	6.7
30-39	1,031 (4.6)	471 (4.1)	2.2	3,145 (5.2)	6.7
40-49	1,611 (7.2)	783 (6.8)	2.1	4,588 (7.6)	5.9
50-59	2,769 (12.3)	1,402 (12.1)	2.0	7,831 (13.0)	5.6
60-69	4,852 (21.6)	2,478 (21.4)	2.0	13,119 (21.8)	5.3
70-79	6,059 (27.0)	3,176 (27.5)	1.9	16,266 (27.1)	5.1
80-89	3,471 (15.4)	2,014 (17.4)	1.7	8,842 (14.7)	4.4
90+	702 (3.1)	467 (4.0)	1.5	1,686 (2.8)	3.6

* Average intensity of transfusion (units per patient per year) per age group

7.2.1. Age distribution of red blood cell recipients

The average age at the time of transfusion was 63.0 years (SD 21.0 years), the oldest average age of patients transfused for any of the blood component types. Variation in red blood cell use by age group is described in Table 7.3, and is illustrated by age and gender in Figure 7.1. The rates of transfusion obtained from the study data were applied to the population age structure for Scotland in the year 2000, accounting for the appropriate proportion of the population that is transfused based on the study data (Figure 7.2). The age group 70-79 years had the largest number of patients and had the largest share (27.1%) of total red blood cell units used. However, those patients in age bands 10-39 years received the highest number of red blood cell units per patient (6.7) over the period of one year (Figure 7.1).

Figure 7.1 **Average red blood cell units used per patient by age group and gender**

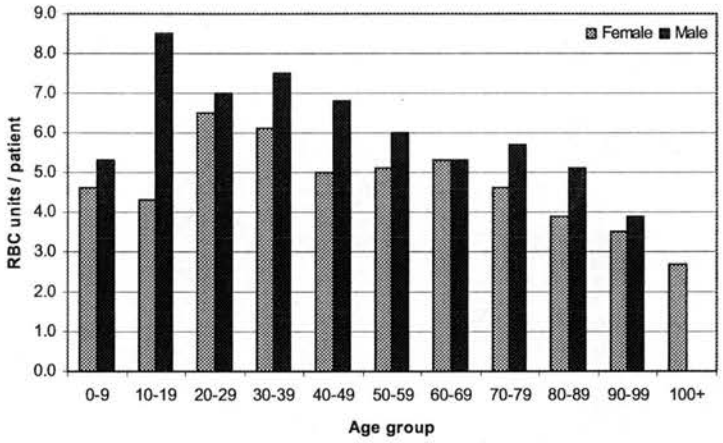
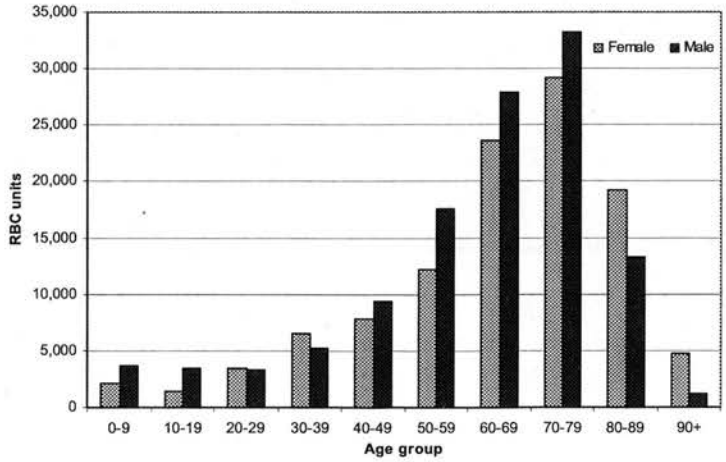


Figure 7.2 **Red blood cell units use by age group and gender for all Scotland in 2000**



7.2.2. Distribution of intensity of transfusion of red cell recipients

The distribution of red blood cell units and red cell recipients transfused by intensity is reported (Table 7.5a). The most common intensity of red blood cell use accounted for by 34.8% of patients, was two units per patient per year. 25,416 red blood cell units were used by 1,311 red cell recipients transfused at an intensity of ten or more units per patient per year, that is, 11.3% of red cell recipients were transfused with ten or more units during the year which accounts for 42.3% of the total red blood cell units used in the study (Table 7.5b). The number of patients transfused with zero red blood cell units but transfused with other blood components was 427, 3.6% of patients in the study dataset

Table 7.5a Intensity of red blood cell use

Units/ patient / year	RBC units (%) n=60,130	Patients (%) n=11,567
1	668 (1.1)	668 (5.8)
2	8,054 (13.4)	4,027 (34.8)
3	4,896 (8.1)	1,632 (14.1)
4	6,856 (11.4)	1,714 (14.8)
5	3,505 (5.8)	701 (6.1)
6	3,714 (6.2)	619 (5.4)
7	2,464 (4.1)	352 (3.0)
8	2,640 (4.4)	330 (2.9)
9	1,917 (3.2)	213 (1.8)
10-19	11,732 (19.5)	898 (7.8)
20-29	5,369 (8.9)	225 (1.9)
30-39	3,038 (5.1)	92 (0.8)
40-49	1,933 (3.2)	45 (0.4)
≥50	3,344 (5.6)	51 (0.4)

Table 7.5b Summary of intensity of red blood cell use

Intensity	1-4 units	5-9 units	≥10 units
Red blood cell units (%) n=60,130	34.0	23.7	42.3
Red blood cell recipients (%) n=11,567	69.5	19.2	11.3

7.3. PLATELET USE

In the study dataset there were 4,084 transfusion day records of at least one unit of platelets used representing 1,422 patients (platelet recipients) and 4,795 used platelet units. 57.0% of these patients were males who accounted for the use of 57.4% of platelet units. On average patients had 2.9 transfusion day records of platelet use and the average intensity of platelet use was 3.4 units per patient per year. These patients also used 6,708 red blood cell units, 3,286 fresh frozen plasma units and 1,041 cryoprecipitate units. 14.3% of transfusion day records of used platelet units and 15.7% of platelet recipients were transfused with platelets only (Table 7.2).

7.3.1. Age distribution of platelet recipients

The average age of patients with transfusion day records of used platelet units was 51.9 years (SD 21.8 years). Variation in platelet use by age group is described in Table 7.6. As for red blood cell use, age group 70-79 years was the largest in terms of the number of patients (24.0%) but age group 60-69 years, which also accounted for the largest proportion of transfusion day records (23.3%), received the largest share (22.9%) of total platelet units used by age group. Patients in age band 30-39 years used the highest number of platelet units used per patient (5.7) and platelet use per patient was particularly predominant in females for this age group (Figure 7.3). The age and gender specific rates of platelet transfusion were applied to the population age structure of Scotland for year 2000 for the appropriate proportion of transfusion recipients to illustrate total platelet use by age and gender for Scotland (Figure 7.4).

The data presented in Table 7.6, and Figures 7.3a and 7.4a, includes all platelet recipients but the data suggests that there are female patients in age group 30-39 years with extreme values for platelet use which may lead to a misrepresentation of platelet use overall. The outlying values for platelet use per patient were considered to be 26 units, 39 units and 90 units. These patients were also transfused with a total of 145 red blood cell units, 25 FFP units and ten cryoprecipitate units. Together the "outlier" patients were linked to 47 SMR01-CD

records and 156 transfusion day records. One patient had a primary diagnosis code (ICD-10) in their first SMR01-CD record in the study dataset for aplastic anaemia and two had diagnosis codes for acute myeloid leukaemia; the procedural codes were blood transfusion, bone marrow extraction and central venous catheter insertion. No date of death was available for these patients at the time of data extraction. Data after the removal of these outliers are shown in Figures 7.3b and 7.4b.

Table 7.6 Population transfused with platelets by age group

Age group Years	**TDR (%)** n=4,084	**Patients (%)** n=1,422	**TDR / Patient**	**PLT units (%)** n=4,795	**PLT units/ Patient ***
0-9	327 (8.0)	75 (5.3)	4.4	339 (7.1)	4.5
10-19	139 (3.4)	35 (2.5)	4.0	160 (3.3)	4.6
20-29	256 (6.3)	64 (4.5)	4.0	297 (6.2)	4.6
30-39	360 (8.8)	80 (5.6)	4.5	459 (9.6)	5.7
40-49	425 (10.4)	156 (11.0)	2.7	509 (10.6)	3.3
50-59	754 (18.5)	221 (15.5)	3.4	876 (18.3)	4.0
60-69	952 (23.3)	326 (22.9)	2.9	1,098 (22.9)	3.4
70-79	670 (16.4)	341 (24.0)	2.0	797 (16.6)	2.3
80-89	194 (4.8)	119 (8.4)	1.6	253 (5.3)	2.1
90+	7 (0.2)	5 (0.4)	1.4	7 (0.1)	1.4

* Average intensity of transfusion (units per patient per year) per age group

Figure 7.3 Average platelet units used per patient by age group and gender

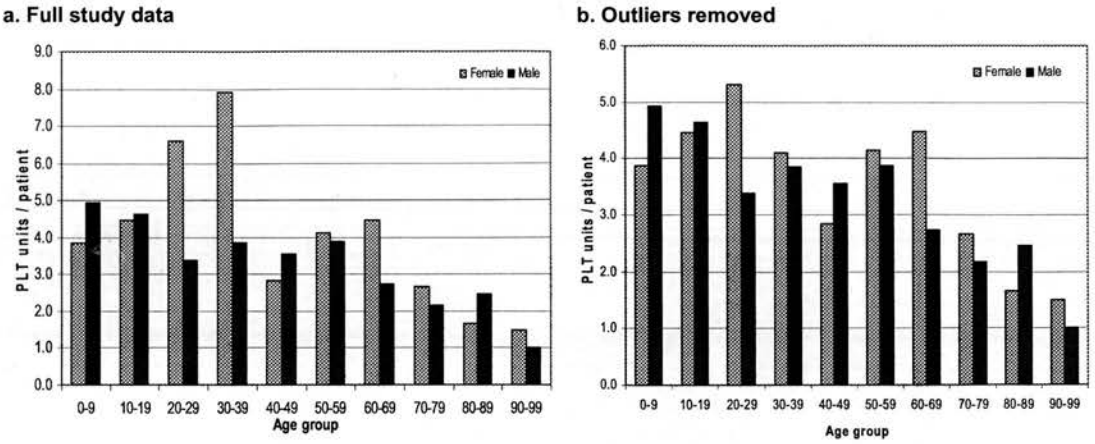
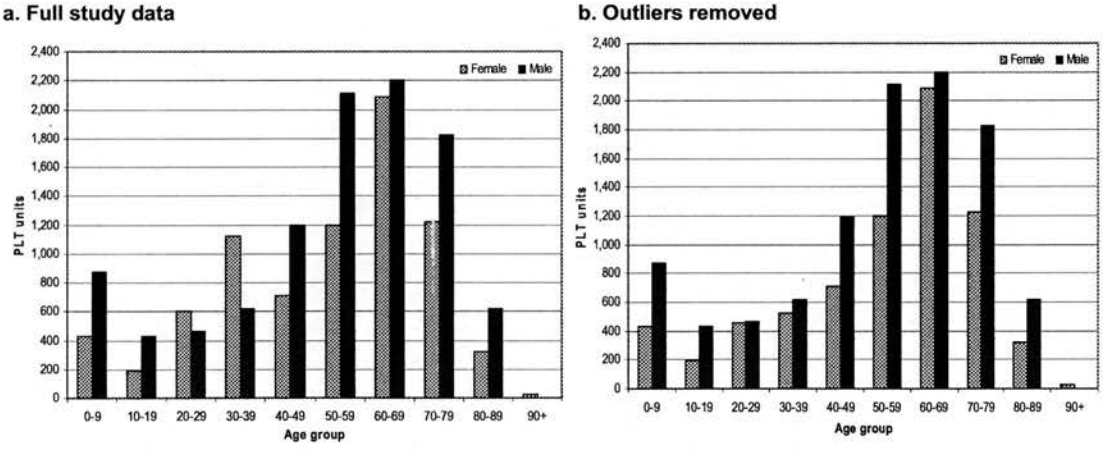


Figure 7.4 Platelet units used by age group and gender for all Scotland in 2000



7.3.2. Distribution of intensity of transfusion of platelet recipients

The distribution of used platelet units and platelet recipients by intensity of platelet use demonstrated that 53.0% of platelet recipients received one unit of platelets per patient per year (Table 7.7a). 6.8% of platelet recipients received ten or more units during the year, accounting for 42.4% of the total platelet units used in the study (Table 7.7b). This echoes the pattern for red blood cell use in which a few patients were transfused intensively and accounted for a large proportion of units used. 88.1% of patients in the study were not transfused with platelet units.

Table 7.7a Intensity of platelet use

Units/ patient / year	PLT units (%) n=4,795	Patients (%) n=1,422
1	754 (15.7)	754 (53.0)
2	468 (9.8)	234 (16.5)
3	408 (8.5)	136 (9.6)
4	280 (5.8)	70 (4.9)
5	215 (4.5)	43 (3.0)
6	162 (3.4)	27 (1.9)
7	196 (4.1)	28 (2.0)
8	136 (2.8)	17 (1.2)
9	144 (3.0)	16 (1.1)
10-19	838 (17.5)	60 (4.2)
20-29	549 (11.4)	24 (1.7)
30-39	212 (4.4)	6 (0.4)
40-49	83 (1.7)	2 (0.1)
≥50	350 (7.3)	5 (0.4)

Table 7.7b Summary of intensity of platelet use

Intensity	1-4 units	5-9 units	≥10 units
Platelet units (%) n=4,795	39.8	17.8	42.4
Platelet recipients (%) n=1,422	84.0	9.2	6.8

7.4. FRESH FROZEN PLASMA USE

The study dataset contained 2,171 transfusion day records of at least one used unit of fresh frozen plasma (FFP). These records represent 1,266 patients (FFP recipients), with an average of 1.7 records of FFP use per patient and an average intensity of FFP use of 7.5 units per patient per year, the highest average transfusion rate of all blood components. 62.8% of FFP recipients were male and accounted for 66.8% of used FFP units, the highest proportions across all blood components. FFP recipients also used 6,777 red blood cell units, 1,140 platelet units and 1,252 cryoprecipitate units. 155 (12.2%) patients transfused with FFP received no other blood component, that is were transfused with FFP only (Table 7.2).

7.4.1. Age distribution of fresh frozen plasma recipients

The average age of patients transfused with fresh frozen plasma was 57.2 years (SD 18.3 years). The variation in FFP use by age group and by gender is reported (Table 7.8 and Figure 7.5). Age group 70-79 years had the largest proportion (26.5%) of patients, as was the case for both red cell and platelet transfusion. Almost half of all FFP recipients (49.2%) were aged 60-69 and 70-79 years. However, the age group that received the highest number of FFP units per patient (20.3) during the study period as well as the largest share of total FFP units used (28.5%) was 40-49 years, younger than for red blood cell or platelet use. The highest intensity of transfusion (20.3) is more than double the next highest (10.0 FFP units per patient per year for age group 20-29 years) and more than eleven times the lowest (1.8 FFP units per patient per year for age group 0-9 years). Total FFP use by age and gender for the whole of Scotland in the year 2000 was quantified (Figure 7.6).

The data presented in Table 7.8, and Figures 7.5a and 7.6a, includes all patients transfused with at least one unit of FFP during the study year. The data indicates that for males aged 40-49 years there are large, outlying values for FFP use that could cause FFP use overall to be misinterpreted.

Table 7.8 Population transfused with fresh frozen plasma by age group

Age group Years	TDR (%) n=2,171	Patients (%) n=1,266	TDR / Patient	FFP units (%) n=9,446	FFP units/ Patient *
0-9	44 (2.0)	34 (2.7)	1.3	62 (0.7)	1.8
10-19	42 (1.9)	27 (2.1)	1.6	142 (1.5)	5.3
20-29	91 (4.2)	49 (3.9)	1.9	490 (5.2)	10.0
30-39	151 (7.0)	77 (6.1)	2.0	622 (6.6)	8.1
40-49	451 (20.8)	133 (10.5)	3.4	2,694 (28.5)	20.3
50-59	336 (15.5)	181 (14.3)	1.9	1,501 (15.9)	8.3
60-69	442 (20.4)	287 (22.7)	1.5	1,902 (20.1)	6.6
70-79	439 (20.2)	336 (26.5)	1.3	1,515 (16.0)	4.5
80-89	164 (7.6)	134 (10.6)	1.2	490 (5.2)	3.7
90+	11 (0.5)	8 (0.6)	1.4	28 (0.3)	3.5

* Average intensity of transfusion (units per patient per year) per age group

The outlying values for FFP use per patient are 76 units, 145 units and 1,776 units: the patients were also transfused with a total of 112 red blood cell units, five platelet units and ten cryoprecipitate units. Together the three patients had 255 transfusion day records of units used and 19 SMR01-CD records. One patient had a primary diagnosis codes (ICD-10), in their first SMR01-CD record in the study database, for chronic renal failure and unspecified renal failure; another patient was diagnosed with thrombotic microangiopathy; the third was diagnosed with thrombotic microangiopathy and thrombocytopenia. The respective procedural codes for these patients were: plasma transfusion, upper gastrointestinal tract endoscopy and total splenectomy. Figures 7.5b and 7.6b report FFP use by age group and gender with these outliers removed.

Figure 7.5 Average FFP units used per patient by age group and gender

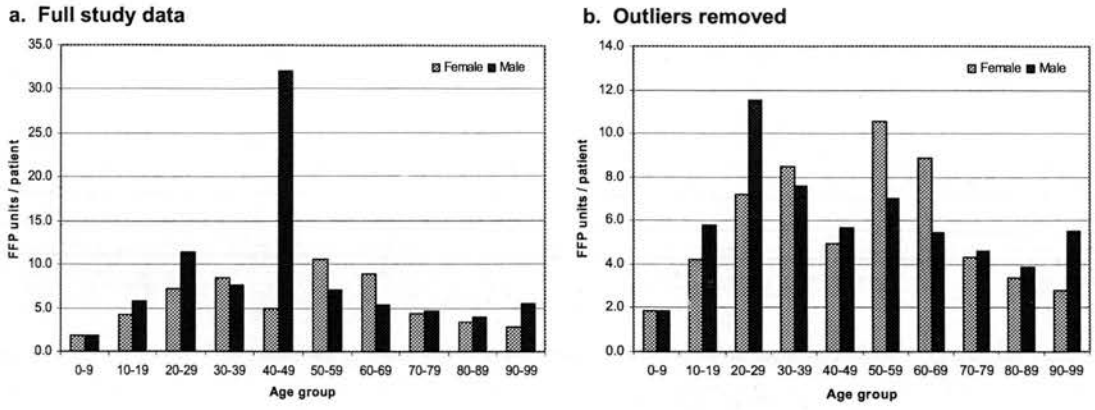
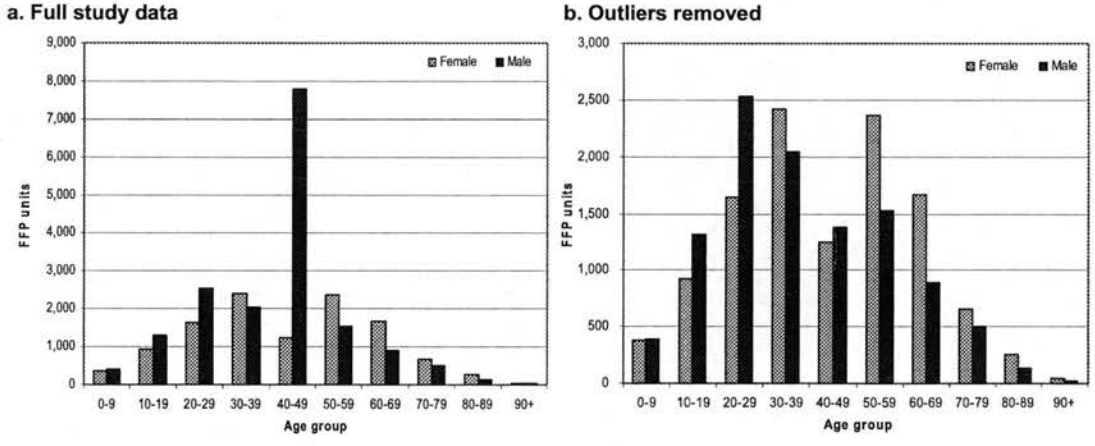


Figure 7.6 FFP units used by age group and gender for all Scotland in 2000



7.4.2. Distribution of intensity of transfusion of fresh frozen plasma

The variation in the number of FFP units used per patient in a year shows that the most common intensity of transfusion for FFP, received by 27.4% of FFP recipients, was three units per patient per year, the highest mode of intensity of all blood components in the study (Table 7.9a). 10.8% of patients transfused with FFP used ten or more units in the year, accounting for 56.3% of all units of FFP used in the study (Table 7.9b). 35.6% of units were transfused at an intensity of 50 or more FFP units per patient per year to 15 patients. The intensity of FFP use is explored further in relation to thrombotic thrombocytopenic purpura, a condition characterised by abnormal platelet clot formation, for which the normal treatment protocol implicates high use of FFP transfusion (section 10.5). 89.4% of all patients in the study were transfused with blood component types other FFP.

Table 7.9a Intensity of fresh frozen plasma use

Units/ patient / year	FFP units (%) n=9,446	Patients (%) n=1,266
1	33 (0.3)	33 (2.6)
2	552 (5.8)	276 (21.8)
3	1,041 (11.0)	347 (27.4)
4	948 (10.0)	237 (18.7)
5	270 (2.9)	54 (4.3)
6	480 (5.1)	80 (6.3)
7	245 (2.6)	35 (2.8)
8	320 (3.4)	40 (3.2)
9	243 (2.6)	27 (2.1)
10-19	1,190 (12.6)	94 (7.4)
20-29	495 (5.2)	21 (1.7)
30-39	175 (1.9)	5 (0.4)
40-49	91 (1.0)	2 (0.2)
≥50	3,363 (35.6)	15 (1.2)

Table 7.9b Summary of intensity of FFP use

Intensity	1-4 units	5-9 units	≥10 units
FFP units (%) n=9,446	27.2	16.5	56.3
FFP recipients (%) n=1,266	70.5	18.7	10.8

7.5. CRYOPRECIPITATE USE

328 transfusion day records of at least one used unit of cryoprecipitate represent 253 patients (cryoprecipitate recipients) and 1,759 used cryoprecipitate units in the study dataset. 61.6% of cryoprecipitate recipients were males who accounted for 62.0% of all cryoprecipitate units used in the study. Patients transfused with cryoprecipitate also used 2,502 red blood cell units, 387 platelet units and 1,278 units of fresh frozen plasma. Patients had an average of 1.3 transfusion day records of cryoprecipitate use and average intensity of transfusion of 7.0 units of cryoprecipitate per year. Three cryoprecipitate recipients (1.2% of all cryoprecipitate recipients) were transfused with cryoprecipitate units only, the lowest proportion for any blood component (Table 7.2).

7.5.1. Age distribution of cryoprecipitate recipients

The average age of cryoprecipitate recipients was 52.5 years (SD 22.5 years). Variation in cryoprecipitate use by age group is described in Table 7.10, and is illustrated by age and gender in Figures 7.7. Further, cryoprecipitate use by age and gender for all of Scotland is reported, calculated by appropriately applying the rates of cryoprecipitate transfusion to the population age structure for Scotland for 2000 (Figure 7.8). As for all other blood component types, age group 70-79 years accounted for the largest proportion of cryoprecipitate recipients (20.2%) and this was the age group that used the largest proportion (24.0%) of cryoprecipitate units. Patients in age band 20-29 years were transfused at the highest intensity of cryoprecipitate units per patient per year (13.9), and accounted for 15.7% of cryoprecipitate units used.

The data reported in Table 7.10, and Figures 7.7a and 7.8a, includes all patients transfused with at least one unit of cryoprecipitate during the study year. The data indicates areas where there are outlying values for cryoprecipitate use which could lead to the misinterpretation of cryoprecipitate use overall. For males in age group 20-29 the highest number of cryoprecipitate units used per patient was 95. The next highest in this age-sex group was 30 cryoprecipitate units. Figures 7.7b and 7.8b report cryoprecipitate use by age

group and gender with the data for this one patient, identified as a high cryoprecipitate user, removed. This patient had 17 SMR01-CD records and 27 transfusion day records of units used and was also transfused with 47 red blood cell units and three FFP units. The first primary diagnosis (ICD-10) recorded in the study dataset (patient's second SMR01 record in 2000) was polyarteritis nodosa, an autoimmune condition characterised by inflammation of blood vessels notably affecting the skin, liver, heart and kidneys. During that admission the patient also underwent a kidney biopsy procedure.

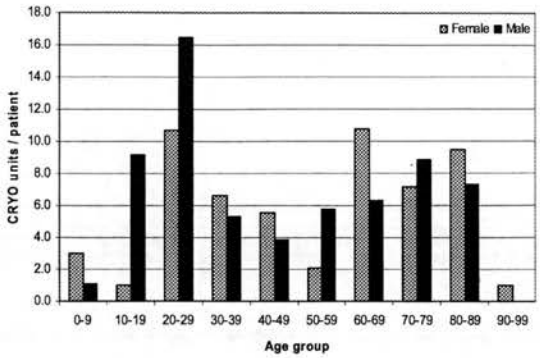
Table 7.10 Population transfused with cryoprecipitate by age group

Age group Years	**TDR (%)** n=328	**Patients (%)** n=253	**TDR / Patient**	**CRYO units (%)** n=1,759	**CRYO units/ Patient ***
0-9	21 (6.4)	17 (6.7)	1.2	34 (1.9)	2.0
10-19	8 (2.4)	8 (3.2)	1.0	57 (3.2)	7.1
20-29	36 (11.0)	20 (7.9)	1.8	277 (15.7)	13.9
30-39	28 (8.5)	24 (9.5)	1.2	146 (8.3)	6.1
40-49	38 (11.6)	31 (12.3)	1.2	147 (8.4)	4.7
50-59	45 (13.7)	39 (15.4)	1.2	184 (10.5)	4.7
60-69	63 (19.2)	44 (17.4)	1.4	345 (19.6)	7.8
70-79	67 (20.4)	51 (20.2)	1.3	423 (24.0)	8.3
80-89	21 (6.4)	18 (7.1)	1.2	145 (8.2)	8.1
90+	1 (0.3)	1 (0.4)	1.0	1 (0.1)	1.0

* Average intensity of transfusion (units per patient per year) per age group

Figure 7.7 Average cryoprecipitate units used per patient by age group and gender

a. Full study data



b. Outlier removed

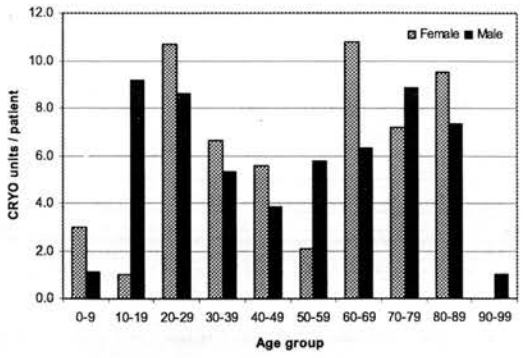
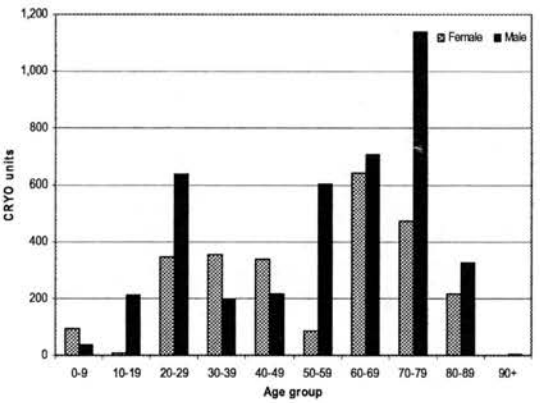
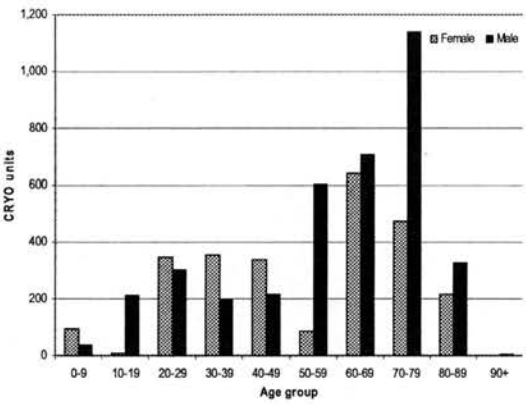


Figure 7.8 Cryoprecipitate units used by age group and gender for all Scotland in 2000

a. Full study data



b. Outlier removed



7.5.2. Distribution of intensity of cryoprecipitate use

Intensity of cryoprecipitate transfusion is reported in Table 7.11a. The most common intensity of transfusion, representing 38.3% of patients, was one cryoprecipitate unit per patient per year. 25.3% of patients used ten units of cryoprecipitate per patient per year, representing the largest share (36.4%) of cryoprecipitate units used in the study. Like the distribution of transfusion intensity for all other blood components, a large proportion of units was used by an intensely transfused minority: 82.1% of cryoprecipitate units were transfused at an intensity of ten or more units per patient per year to 37.6% of cryoprecipitate recipients (Table 7.11b). The mode number of units per transfusion day record and mode number of units per patient for cryoprecipitate use regardless of other blood component units used is one, and for cryoprecipitate use alone is 10 suggesting that when patients receive cryoprecipitate units only they receive many more units when compared to patients transfused with cryoprecipitate units who may also receive other blood components (Table 7.2). This disparity may represent the transfusion of cryoprecipitate units for different clinical reasons. 97.9% of patients in the study did not receive cryoprecipitate transfusion.

Table 7.11a Intensity of cryoprecipitate use

Units/ patient / year	CRYO units (%) n=1,759	Patients (%) n=253
1	97 (5.5)	97 (38.3)
2	56 (3.2)	28 (11.1)
3	27 (1.5)	9 (3.6)
4	32 (1.8)	8 (3.2)
5	10 (0.6)	2 (0.8)
6	54 (3.1)	9 (3.6)
7	14 (0.8)	2 (0.8)
8	24 (1.4)	3 (1.2)
10	640 (36.4)	64 (25.3)
11-19	165 (9.4)	12 (4.7)
20	200 (11.4)	10 (4.0)
≥21	440 (25.0)	9 (3.6)

Table 7.11b Summary of intensity of cryoprecipitate use

Intensity	1-4 units	5-9 units	≥10 units
Cryoprecipitate units (%) n=1,759	12.1%	5.8%	82.1%
Cryoprecipitate recipients (%) n=253	56.1%	6.3%	37.6%

7.6. OVERVIEW OF BLOOD COMPONENT USE

The findings reported here in Chapter 7 address the objective of analysing the demographics of patients transfused with each blood component for the study population in order to show that the study dataset can be utilised in this way. Here the demographics of transfusion recipients and the use of blood component units for the sub-groups of recipients by blood component type are described.

The findings identify high users by age group and gender as well as individual patients with blood component use considered to be of outlying value in comparison with rates by age and gender overall. Further, the number of units used per age group and gender was applied to the appropriate proportion of transfusion population for the population age structure of Scotland in the year 2000 to quantify the population's use of blood by age and gender.

Table 7.12 Summary of intensity of transfusion for each blood component

Statistic	Transfusion day records of units used			
	RBC	PLT	FFP	CRYO
Modal intensity (units used per patient per year)	2	1	3	1
Percentage of units transfused	13.4	15.7	11.0	5.5
Percentage of patients transfused	34.8	53.0	27.4	38.3
Intensity level < 10 units per patient per year				
Percentage of units transfused	57.7	57.6	43.7	17.9
Percentage of patients transfused	88.7	93.2	89.2	62.4
Intensity level ≥ 10 units per patient per year				
Percentage of units transfused	42.3	42.4	56.3	82.1
Percentage of patients transfused	11.3	6.8	10.8	37.5

Distributions of patients and units by intensity of transfusion are summarised for the proportion of patients and units transfused for the mode intensity, for the intensity level of ten or more units per patient per year, and the intensity level of less than ten units per patient per year, for each blood component (Table 7.12). The findings show that for the

mode intensity, that is, the most common number of units used per patient per year, the proportion of patients transfused at this level is greater than the proportion of units used whereas for intensity level ten or more units per patient per year the proportion of units used is greater than the proportion of patients transfused at this level. In summary, this indicates that many patients are transfused at a low intensity and the total units accounted for is small, and conversely, few people are transfused intensively accounting for a large proportion of the units used.

The findings of analyses of blood use by clinical case group, specifically, surgical red cell using procedures (Chapter 8) and by haematological conditions (Chapter 9), are described and illustrated in subsequent chapters.

8. RESULTS: RULE FOR ATTRIBUTING BLOOD USE TO SURGICAL PROCEDURE CASE GROUPS

8.1. INTRODUCTION

The findings reported in previous chapters (Chapters 6 and 7) have shown that transfusion day records and SMR01-CD records can be linked to create a dataset that can be used to describe the groups of patients who use blood components. Further, this study aimed to utilise the dataset to describe the use of blood by clinical case groups that represent the clinical reasons that are likely to explain the patient's underlying requirement for red blood cell transfusion. The specific methods employed were described in full elsewhere (section 5.3.1).

Previous published reports described the use of blood for various categories of surgical intervention and stated surgery to be a notable area of blood use. The development of strategies for the conservation of red blood cell use, such as the implementation of MSBOS, support the assessment of blood use for surgical events as an important requirement for informing the clinical and transfusion practice. As such a surgical blood attribution rule incorporating temporal and clinical factors was defined and validated for use in attributing transfusion day records of red blood cell units used to specified red cell using procedures (Table 5.4). The attribution was made if the date of transfusion fell during the period starting seven days prior to admission and ending on the date of discharge and if the SMR01-CD record that satisfied that date rule contained a coding for a red cell using procedure specified for this study.

The findings reported here describe red blood cell use for transfusion day records that can be attributed to only one red cell using procedure (section 8.2) and red blood cell use for transfusion day records that can be attributed to more than one red cell using procedure, that is, the findings of the investigations into inter-episode competition (section 8.3). Finally an overview of all results is provided in which instances of inter-episode competition were resolved according to the surgical blood attribution rules (section 8.4).

In total the study dataset contained 22,471 transfusion day records of red blood cell units used (85.5% of all transfusion day records of any component use) that represented 11,567 patients. A summary of the number of transfusion day records of red blood cell units used, patients and red blood cell units used, as well as patient demographics for the different subgroups of findings just described (and reported in the following sections) is given in Table 8.1. Data for transfusion day records of red blood cell use that can be attributed to one red cell using procedure and those that can be attributed to more than one red cell using procedure are reported both separately and combined, along with the data for transfusion day records of red blood cell use that cannot be attributed to any red cell using procedure in this study.

Table 8.1 Summary of findings for the attribution of blood to red cell using procedures

Statistic	Attributed by surgical blood attribution rule to ...			
	One RBC using procedure (section 8.2)	**More than 1 RBC using procedure** (section 8.3)	**One or more RBC using procedures** (section 8.4)	**No RBC using procedures**
Patients	4,282	28	4,293	7,790
Transfusion day records	5,841	41	5,882	16,589
Sex (% male)	48.7	61.0	48.8	50.9
Age in years (range)	0-101.1	2.7-88.4	0-101.1	0-101.4
Age in years (mean, SD)	67.1, 16.2	50.6, 22.3	67.0, 16.3	61.6, 22.3
RBC units used	17,122	281	17,403	42,727

8.2. RED BLOOD CELL USE ATTRIBUTED TO A SINGLE SMR01-CD RECORD THAT CONTAINS A RED CELL USING PROCEDURE

Table 8.2 Red blood cell use by procedure where blood can be attributed to a single SMR01-CD record containing a red cell using procedure

Red cell using procedure	RBC units used (% RBC use) n=17,122	TDR (% TDR) n=5,841	Units/ TDR
Open bypass graft operations (minus revisions)	3,634 (21.2)	1,240 (21.2)	2.9
Total hip replacement (minus revisions)	1,766 (10.3)	800 (13.7)	2.2
Operations on valves of heart and adjacent structures	1,383 (8.1)	395 (6.8)	3.5
Open reduction of fracture	1,294 (7.6)	512 (8.8)	2.5
Excision of colon	1,279 (7.5)	462 (7.9)	2.8
Other operations on aorta	950 (5.5)	240 (4.1)	4.0
Closed reduction of fracture	947 (5.5)	366 (6.3)	2.6
Emergency replacement of aneurysmal segment of aorta	843 (4.9)	112 (1.9)	7.5
Excision of rectum	762 (4.5)	268 (4.6)	2.8
Total hip replacement revisions	731 (4.3)	230 (3.9)	3.2
Total knee replacement (minus revisions)	522 (3.0)	243 (4.2)	2.1
Replacement of head of femur	483 (2.8)	236 (4.0)	2.0
Hysterectomy	421 (2.5)	152 (2.6)	2.8
Transplantation of liver	395 (2.3)	44 (0.8)	9.0
Other open operations on kidney	307 (1.8)	97 (1.7)	3.2
Partial excision of liver	280 (1.6)	55 (0.9)	5.1
Open operations on oesophagus	277 (1.6)	102 (1.7)	2.7
Operations on tissue of brain	272 (1.6)	75 (1.3)	3.6
Excision of lung	120 (0.7)	55 (0.9)	2.2
Open operations on prostate	116 (0.7)	35 (0.6)	3.3
Total knee replacement revisions	97 (0.6)	42 (0.7)	2.3
Transplantation of kidney	84 (0.5)	25 (0.4)	3.4
Open bypass graft operations revisions	58 (0.3)	14 (0.2)	4.1
Reconstruction of renal artery	54 (0.3)	19 (0.3)	2.8
Other operations on lung	23 (0.1)	12 (0.2)	1.9
Operations on thyroid or parathyroid glands	21 (0.1)	8 (0.1)	2.6
Open extirpation of lesion of lung	3 (<0.1)	2 (<0.1)	1.5

Note: Transplantation of heart (including transplantation of heart and lung) not coded in any SMR01-CD record in study dataset and so blood component use could not be attributed to that procedural case group

5,841 transfusion day records of red blood cell use could be attributed to a single SMR01-CD record that contained a red cell using procedure. These events accounted for 17,122 red blood cell units used (28.5% of used red blood cell units in the study dataset) and relate to 4,282 patients with an average age of 67.1 years (SD 16.2, range 0-101.1 years) and of whom 48.7% are male (Table 8.1). The results for the number of red blood cell units used, number of transfusion day records and red blood cell units used per transfusion day record where blood can be attributed to a single red cell using procedure are reported in Table 8.2. In this analysis the largest proportion of blood was attributed to primary open bypass graft operations (excluding revisions) (21.2% of RBC units attributed to a single red cell using procedure). The highest value for the average number of red blood cell units used per transfusion day record was 9.0 units, for liver transplant procedures (Table 8.2).

8.3. RED BLOOD CELL USE ATTRIBUTED TO TWO COMPETING SMR01-CD RECORDS THAT EACH CONTAINS A RED CELL USING PROCEDURE

By applying the surgical blood attribution rule to the study dataset there was the potential for a transfusion day record of red blood cell units used to be linked with more than one SMR01-CD record that contained a red cell using procedure: the extent to which such inter-episode competition (Figure 5.4) occurred in the study was assessed and the results reported here.

41 transfusion day records of red blood cell use were attributed to more than one SMR01-CD record that contained a red cell using procedure and in all cases each transfusion day record was attributed to two SMR01-CD records, thereby being attributed to two red cell using procedures. These cases of inter-episode competition represented 28 patients with an average age of 50.6 years (SD 22.3, range 2.7-88.4 years) and of whom 61.0% are male: patients was younger and had a higher proportion of males than the group of patients for whom transfusion day records were attributed to a single red cell using procedure (Table 8.1). Red blood cell use by the first occurring red cell using procedure is reported (Table 8.3) and is explored in further detail by combination of competing procedures (Table 8.4).

Table 8.3 Red blood cell use by procedure for cases of inter-episode competition: by patient's first occurring red cell using procedure

Red cell using procedure	RBC units used (% RBC use) n=281	TDR (% TDR) n=41	Units/ TDR
Other operations on aorta	79 (28.1)	6 (14.6)	13.2
Open of reduction fracture	71 (25.3)	7 (17.1)	10.1
Transplantation of liver	52 (18.5)	6 (14.6)	8.7
Operations on tissue of brain	36 (12.8)	7 (17.1)	5.1
Excision of rectum	10 (3.6)	1 (2.4)	10.0
Excision of colon	9 (3.2)	3 (7.3)	3.0
Operations on valves of heart and adjacent structures	8 (2.8)	2 (4.9)	4.0
Open operations on oesophagus	4 (1.4)	2 (4.9)	2.0
Closed of reduction fracture	4 (1.4)	2 (4.9)	2.0
Total hip replacement (minus revisions)	2 (0.7)	2 (4.9)	1.0
Total knee replacement (minus revisions)	2 (0.7)	1 (2.4)	2.0
Open bypass graft operations (minus revisions)	2 (0.7)	1 (2.4)	2.0
Hysterectomy	2 (0.7)	1 (2.4)	2.0

Table 8.4 Red blood cell use by procedure for cases of inter-episode competition: by combination of competing procedures

Red cell using procedure combinations	RBC units used (% RBC use) n=281	TDR (%TDR) n=41	Units/ TDR
Two procedures are the same			
Open reduction of fracture	71 (25.3)	7 (17.1)	10.1
Transplantation of liver	39 (13.9)	3 (7.3)	13.0
Other operations on aorta	9 (3.2)	2 (4.9)	4.5
Operations on valves of heart and adjacent structures	8 (2.8)	2 (4.9)	4.0
Open operations on oesophagus	4 (1.4)	2 (4.9)	2.0
Total hip replacement (minus revisions)	3 (1.1)	2 (4.9)	1.5
Excision of colon	3 (1.1)	1 (2.4)	3.0
Operations on tissue of brain	3 (1.1)	1 (2.4)	3.0
Subtotal (Two procedures are the same)	**140 (49.8)**	**20 (48.8)**	
Two procedures are related			
Excision of colon / Excision of rectum	6 (2.1)	2 (4.9)	3.0
Closed reduction fracture / Open reduction fracture	4 (1.4)	2 (4.9)	2.0
Total hip replacement (minus revisions) / Total hip replacement revisions	1 (0.4)	1 (2.4)	1.0
Subtotal (Two procedures are related)	**11 (3.9)**	**5 (12.2)**	
Two procedures are not related			
Other operations on aorta / Excision of colon	41 (14.6)	2 (4.9)	20.5
Other operations on aorta / Excision of rectum	39 (13.9)	3 (7.3)	13.0
Operations on tissue of brain / Transplantation of liver	33 (11.7)	6 (14.6)	5.5
Operations on tissue of brain / Open reduction of fracture	13 (4.6)	3 (7.3)	4.3
Open bypass graft operations (minus revisions) / Excision of colon	2 (0.7)	1 (2.4)	2.0
Hysterectomy / Excision of rectum	2 (0.7)	1 (2.4)	2.0
Subtotal (Two procedures are not related)	**130 (46.3)**	**16 (39.0)**	

Cases of inter-episode competition between red cell using procedures accounted for 281 used red blood cell units which equates to 1.6% of all red blood cell units attributed to red cell using procedures and 0.5% of all red blood cell units used in the study. For three red cell using procedures, the number of red blood cell units used per transfusion day record in cases of competition (when procedure was the first red cell using procedure) was much higher than the number of red blood cell units used per transfusion day record when no

competition arose: these were "operations on aorta" (13.2 versus 4.0 RBC units per TDR), "open reduction of fracture" (10.1 versus 2.5 RBC units per TDR) and "excision of rectum" (10.0 versus 2.8 RBC units per TDR) (Tables 8.2 & 8.3). Similarly, there were two combinations of procedures for which the number of red blood cell units used per transfusion day record was much higher than for the procedures involved when there was no competition: these are, competition between "other operations on aorta" and "excision of colon" (20.5 versus 4.0 or 2.8 RBC per TDR), and competition between "other operations on aorta" and "excision of rectum" (13.0 versus 4.0 or 2.8 RBC per TDR), than (Table 8.4).

There were eight different combinations of procedures where the two competing red cell using procedures were in fact the same and competition could evidently be resolved (Table 8.4). These examples accounted for 20 transfusion day records and the use of 140 red blood cell units thereby effectively reducing the number of red blood cell units attributed to competing procedures to 141 (0.8% of red blood cell units attributed to red cell using procedures). There were a further three combinations where the two competing procedures were within the same specialty or could be otherwise related to each other in terms of anatomical site, for example, "excision of colon" and "excision of rectum" are both related to the gastrointestinal tract. If it was considered appropriate to combine competing procedures such as these into single red cell using procedure case groups reflecting the relevant specialty and/or anatomical site then the number of used red blood cell units attributed to competing procedures could be reduced to 130 (0.7% of red blood cell units attributed to red cell using procedures). For the remaining combinations of competing procedures the red cell using procedures could not be instantly or intuitively related to one another and inter-episode competition was considered to be irresolvable.

By addressing inter-episode competition in this way a maximum of 99.3% of used red blood cell units attributed to red cell using procedures could potentially be attributed to a single red cell using procedure case group or related surgical group that may have to be redefined. This result indicates that the issue of competing red blood cell using procedures does not have a large influence on the overall quantification of red cell use in surgery. Therefore, the initial suggestion that transfusion day records be attributed to the first occurring red cell using procedure to satisfy the surgical blood attribution rule was accepted and utilised in subsequent analyses using the surgical blood attribution rule (section 8.4).

8.4. OVERVIEW OF RESULTS FOR ATTRIBUTION OF BLOOD TO SURGICAL CASE GROUPS

The findings reported in this section describe the overall use of red blood cell units in relation to the number of operations performed for the specific group of red cell using procedures defined for this study. Table 8.5 and Figure 8.1 report the overall distribution of the 17,403 transfused red blood cell units that could be attributed to red cell using procedures according to the surgical blood attribution rule defined in this study. In Figure 8.1 the data is reported by surgical category rather than individual procedure.

A total of 5,882 transfusion day records of used red blood cell units, representing 28.9% of the red blood cell units used in the study, could be attributed to red cell using procedures according to the surgical blood attribution rule. In addition, 11.5% of platelet units, and 20.0% of fresh frozen plasma and cryoprecipitate units combined were recorded as transfused in these transfusion day records. 42,727 used red blood cell units could not be attributed to any red cell using procedure by the surgical blood attribution rule.

As was demonstrated in the previous sections the majority of transfusion day records could be attributed to just one red cell using procedure but for a small number there was inter-episode competition between two red blood cell using procedures. The surgical blood attribution rule accounted for competition by attributing red blood cell units to the first red cell using surgical procedure that occurs in the first occurring SMR01-CD record (chronologically) that satisfies the temporal part of the surgical blood attribution rule. Investigation of the nature of competing red cell using procedures was examined and in most cases the competing procedures were the same, or were of similar specialty or anatomical site. By considering these combinations as a single procedural case group, the number of used red blood cell units accounted for by inter-episode competition was just 0.7% of all used red blood cell units attributed to surgical procedures.

The number of operations reported in Table 8.5 is the number of individual procedures carried out during the year 2000 for the relevant study population. These figures were obtained from the denominator data selected from the file of all SMR01-CD records for the whole of Scotland in the year 2000 (ISD, online). The denominator file contains all year 2000

SMR01-CD records (regardless of whether the individual patients could be linked to a transfusion record) for hospitals for which the majority of transfusion events were included in the study dataset. Hospitals for which a small number of transfusion day records appeared in the dataset due to assignments of specially typed blood component units were not included in the denominator file because including them would cause the number of operations performed for the denominator population to be overestimated and would subsequently underestimate the proportion of operations transfused. The number of operations is the number of SMR01-CD records that contain a coding of the relevant procedures: that is, in cases where a single procedure is coded more than once in an SMR01-CD record the procedure is accounted for once and is counted as one operation. The number of red blood cell units used per operation gives an indication of the average rate of transfusion for each procedure, for example, transplant of liver (10.2 red blood cell units per operation performed) appears to be more heavily transfused on average than total hip replacement (1.1 units per operation performed), though more red blood cell units are used overall for total hip replacements because more of them are performed.

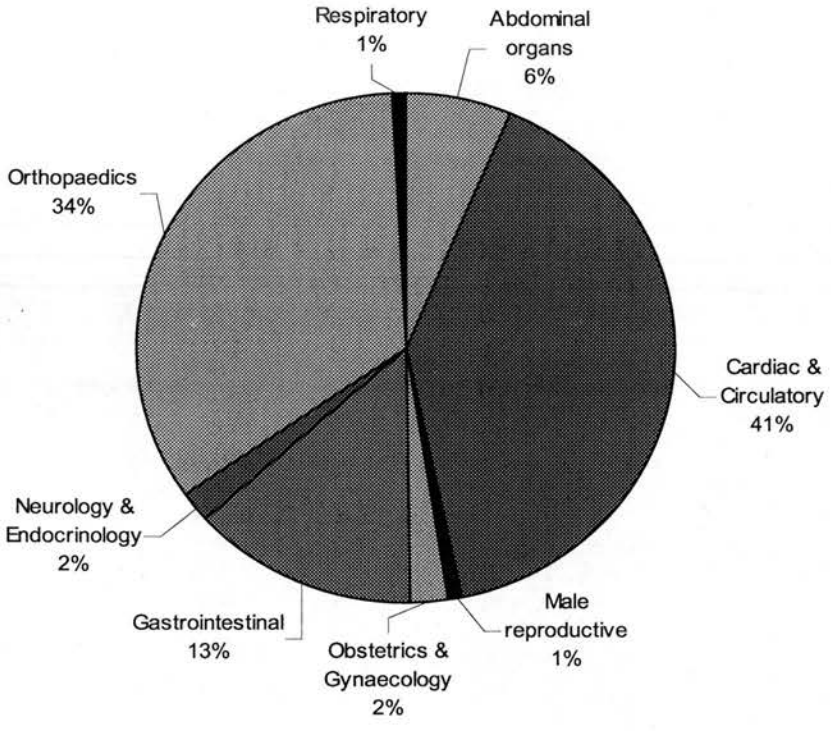
The findings reported here demonstrate that the surgical blood attribution rule defined for the study can successfully attribute the use of red blood cell units to specified surgical case groups that are likely to represent the underlying clinical indication that explains why the patient was transfused. By surgical category mapped roughly to surgical specialty the main areas of red blood cell use are the cardiac and circulatory (41%) and orthopaedic (34%) specialties; the next largest are gastroenterology (13%) and abdominal organs (6%) (Figure 8.1).

The next chapter presents the data for the use of use of blood for chronic haematological conditions hypothesised to be another well-defined set of clinical case groups that can explain a further appreciable proportion of blood use for the study population (Chapter 9).

Table 8.5 Overall results for red blood cell use per operation for red blood cell using procedures

Red cell using procedure	RBC units used (% RBC units) n=17,403	Operations (% operations) n=15,676	Units/ Operation
Transplantation of liver	447 (2.6)	44 (0.3)	10.2
Emergency replacement of aneurysmal segment of aorta	843 (4.8)	104 (0.7)	8.1
Other operations on aorta	1,029 (5.9)	222 (1.4)	4.6
Operations on valves of heart and adjacent structures	1,391 (8.0)	332 (2.1)	4.2
Open bypass graft operations revisions	58 (0.3)	16 (0.1)	3.6
Partial excision of liver	280 (1.6)	82 (0.5)	3.4
Total hip replacement revisions	731 (4.2)	242 (1.5)	3.0
Open bypass graft operations (minus revisions)	3,636 (20.9)	1,241 (7.9)	2.9
Open operations on prostate	116 (0.7)	44 (0.3)	2.6
Open operations on oesophagus	281 (1.6)	171 (1.1)	1.6
Excision of rectum	772 (4.4)	468 (3.0)	1.6
Excision of colon	1,288 (7.4)	837 (5.3)	1.5
Total knee replacement revisions	97 (0.6)	68 (0.4)	1.4
Other open operations on kidney	307 (1.8)	227 (1.4)	1.4
Operations on tissue of brain	308 (1.8)	255 (1.6)	1.2
Total hip replacement (minus revisions)	1,768 (10.2)	1,647 (10.5)	1.1
Transplantation of kidney	84 (0.5)	81 (0.5)	1.0
Replacement of head of femur	483 (2.8)	675 (4.3)	0.7
Total knee replacement (minus revisions)	524 (3.0)	1,022 (6.5)	0.5
Excision of lung	120 (0.7)	239 (1.5)	0.5
Open reduction of fracture	1,365 (7.8)	2,752 (17.6)	0.5
Closed reduction of fracture	951 (5.5)	2,875 (18.3)	0.3
Hysterectomy	423 (2.4)	1,292 (8.2)	0.3
Reconstruction of renal artery	54 (0.3)	167 (1.1)	0.3
Other operations on lung	23 (0.1)	181 (1.2)	0.1
Open extirpation of lesion of lung	3 (<0.1)	24 (0.2)	0.1
Operations on thyroid or parathyroid glands	21 (0.1)	368 (2.3)	0.1

Figure 8.1 Red blood cell units used by red cell using procedure categories



n=17,403 red blood cell units

Category	Red cell using procedure	
Abdominal organs	Transplantation of liver	Transplantation of kidney
	Partial excision of liver	Other open operations on kidney
Cardiac & Circulatory	Valves & adjacent structures	Emergency replacement of aortic aneurysm
	Other operations on aorta	Open bypass graft operations revisions
	Reconstruction of renal artery	Open bypass graft operations (minus revisions)
Neurology & Endocrinology	Thyroid or parathyroid	Operations on tissue of brain
Gastrointestinal	Excision of colon	Open operations on oesophagus
	Excision of rectum	
Male reproductive	Open operations on prostate	
Obstetrics & Gynaecology	Hysterectomy	
Orthopaedics	Open reduction of fracture	Total hip replacement (minus revisions)
	Closed reduction of fracture	Total hip replacement revisions
	Replace head of femur	Total knee replacement (minus revisions)
		Total knee replacement revisions
Respiratory	Excision of lung	Open extirpation of lesion of lung
	Other operations on lung	

9. RESULTS: RULE FOR ATTRIBUTING BLOOD USE TO PATIENTS WITH HAEMATOLOGICAL CONDITIONS

9.1. INTRODUCTION

In Chapter 8 red blood cell use that could be attributed to a group of red cell using procedures was described: 28.9% of red blood cell units in the study dataset were attributed to surgical events. In this chapter the use of blood for diagnostic case groups that may necessitate a high requirement for red blood cells and other blood components is reported. The diagnostic case groups are the malignant haematological conditions lymphoma, myeloma, and leukaemia, and the pre-malignant haematological conditions myelodysplastic syndromes (MDS) and polycythaemia vera (PCV). The blood attribution rule devised for this group of conditions attributed all transfusion events in the study period, that belong to a patient, to one of the haematological case groups if the patient had a coding of one of the specified haematological conditions in any ICD-10 variable at any time during the study period (section 5.3.2). In the event that a patient was diagnosed with more than one of these conditions, blood use was attributed to the first such diagnosis in the patient's SMR01-CD records occurring chronologically during the study period.

The findings of analyses of red blood cell use that could be attributed to a haematological case group (section 9.2) and specifically more than one different haematological case group during the study year (section 9.3) are reported here.

9.2. BLOOD COMPONENT USE LINKED TO PATIENTS WITH DIAGNOSES OF MALIGNANT AND PRE-MALIGNANT HAEMATOLOGICAL CONDITIONS

726 patients with a diagnosis of a pre-malignant or malignant haematological condition could be linked with at least one transfusion day record of used blood component units. The characteristics of patients diagnosed with each condition (referred to as haematological patients, herein) are reported in Table 9.1. Results are reported by patients' first haematological diagnosis in the study which for most cases was the only specified haematological condition that was diagnosed during the study. The patients who were diagnosed with more than one type of haematological condition are explored separately (section 9.3).

The number of SMR01-CD records linked to patients with haematological conditions was quantified in two ways: the total number of SMR01-CD records linked to patients with diagnoses of haematological conditions and the number of SMR01-CD records that contained a coding of a haematological diagnosis. 88.3% of haematological patients' total SMR01-CD records for the year 2000 contain an actual haematological diagnosis. This view of the data is indicative of the hospital activity prior to diagnosis (or potentially following resolution of the relevant condition).

The largest group of haematological patients was those diagnosed with leukaemia. Leukaemia accounted for 36% of all haematological patients, 50.1% of transfusion day records and 39.7% of SMR01-CD records that can be related to haematological diagnoses. Leukaemia patients had the highest proportion of males and the highest average number of transfusion day records per patient. Because of this finding leukaemia patients were assessed separately by type of leukaemia: the two predominant types being lymphoid and myeloid leukaemia (Table 9.2). Patients in the study who were diagnosed with lymphoid leukaemia had on average more inpatient hospital admissions (SMR01-CD records) than others and myeloid leukaemia patients accounted for more transfusion day records.

Table 9.1 Characteristics of patients with a diagnosis of a malignant or pre-malignant haematological condition

	All conditions	Lymphoma	Myeloma	Leukaemia	MDS/PCV
Patients	726	196	126	261	143
Transfusion day records	4,584	964	427	2,324	869
SMR01-CD records (total)	7,063	2,149	1,107	2,731	1,076
SMR01-CD records (haematological)	6,235	1,961	1,033	2,496	745
Sex* (% male)	54.3	49.5	48.4	62.8	50.3
Age* in years (range)	0.8-97.2	4.6-93.0	31.1-93.7	0.8-93.9	19.7-97.2
Age in years (mean, SD)	64.2, 21.4	61.5,18.0	70.8, 11.5	56.1,26.5	76.6,13.1
TDR per patient (range)	1-105	1-49	1-19	1-105	1-62
TDR per patient (mean, SD)	6.31, 9.68	4.92, 6.50	3.39, 3.33	8.90, 12.8	6.10, 9.49
SMR01-CD per patient (range)	1-123	1-80	1-36	1-123	1-50
SMR01-CD per patient (mean, SD)	9.73, 11.5	11.0,12.8	8.79, 6.88	10.5, 13.6	7.52, 7.44

MDS: myelodysplastic syndromes. PCV: polycythaemia vera. * Sex and age by patient

Table 9.2 Patients with a diagnosis of leukaemia

Type of leukaemia	Patients n=261	TDR n=2,324	TDR / Patient	SMR01-CD (haematological) n=2,496	SMR01-CD (total) n=2,731
Lymphoid leukaemia	134	722	5.4	1,494	1,610
Myeloid leukaemia	116	1,497	12.9	939	1,012
Other leukaemias of specified cell type	5	24	4.8	7	34
Other leukaemias of unspecified cell type	6	81	13.5	56	75

A total of 4,584 transfusion day records representing 7,286 used red blood cell units (12.1% of red blood cell units used in study), 2,299 (47.9%) used platelet units, 168 (1.8%) used fresh frozen plasma units and 144 (8.2%) used units of cryoprecipitate could be attributed to the haematological conditions (Table 9.3). Of the 7,286 red blood cell units used 107 (1.5%) could also be attributed to a red cell using procedure as defined for the surgical blood attribution rule (Chapter 8). Blood component use for leukaemia patients by specific type of leukaemia is reported separately in Table 9.4.

Table 9.3 **Blood component use for patients with a haematological diagnosis: by patients' first recorded diagnosis**

Diagnosis	RBC units n=7,286	PLT units n=2,299	FFP units n=168	CRY units n=144	All units n=9,897
Lymphoma	1,639	452	20	1	2,112
Myeloma	953	66	10	20	1,049
Leukaemia *	2,778	1,533	118	113	4,542
MDS/PCV	1,916	248	20	10	2,194

* Blood use by sub-division of Leukaemia reported in Table 9.4

Table 9.4 **Blood component use for patients diagnosed with leukaemia by specific type of leukaemia diagnosed**

Type of leukaemia	RBC units n=2,778	PLT units n=1,533	FFP units n=118	CRY units n=113	All units n=4,542
Lymphoid leukaemia	1,059	388	38	14	1,499
Myeloid leukaemia	1,541	1,106	80	99	2,826
Other leukaemias of specified cell type	65	0	0	0	65
Other leukaemias of unspecified cell type	113	39	0	0	152

9.3. BLOOD COMPONENT USE LINKED TO PATIENTS WITH MORE THAN ONE TYPE OF PRE-MALIGNANT OR MALIGNANT HAEMATOLOGICAL CONDITION

33 transfusion recipients were diagnosed with more than one type of haematological condition during the study period: they accounted for 264 transfusion day records and 434 SMR01-CD records of which 376 contained an actual haematological diagnosis (Tables 9.5 & 9.6). All available SMR01-CD records for the year 2000 for the patients with more than one haematological diagnosis were examined to gain an insight into how the combinations of diagnoses occur and in order to determine whether combinations are clinically relevant. The illustrated examples show how the diagnoses made in SMR01 records change over time and how they relate to the cause of death (Figure 9.1).

Table 9.5 Patients with more than one type of haematological condition diagnosed: by first diagnosis

Diagnosis	Patients n=33	TDR n=264	TDR / Patient	SMR01-CD (haematological) n=376	SMR01-CD (total) n=434
Lymphoma	8	66	8.3	122	126
Myeloma	3	8	2.7	29	31
Leukaemia	6	45	7.5	95	99
MDS/PCV	16	145	9.1	130	178

Table 9.6 Patients with more than one type of haematological condition diagnosed: by combination of diagnosis

Diagnosis combinations *	Patients n=33	TDR n=264	TDR / Patient	SMR01-CD (haematological) n=376	SMR01-CD (total) n=434
Leukaemia & Myeloma	4	15	3.8	92	91
Lymphoma & Leukaemia	8	41	5.1	91	88
Lymphoma & MDS/PCV	2	34	17.0	12	10
Myeloma & MDS/PCV	2	4	2.0	20	18
Leukaemia & MDS/PCV	17	170	10.0	219	169

* Order reported in table does not reflect order in SMR01-CD records i.e. leukaemia & myeloma does not relate only to situations where leukaemia is the diagnosis made before myeloma, rather includes all instances of leukaemia & myeloma or myeloma & leukaemia combined diagnoses.

In the first example, the patient had four consultant episodes within a period of 44 days and received a total of 14 red blood cell units. The diagnosis reported in the SMR01 records of the first three consultant episodes was classified in this study as lymphoma, which changed to leukaemia in the fourth consultant episode. However, the fourth consultant episode finished when the patient died at which point the cause of death was recorded as unspecified peripheral & cutaneous T-cell lymphomas. The difference between the diagnoses could reflect uncertainties in classifying the diagnosis or reflect perceived changes in the manifestation of the disease as the condition progresses. Uncertainty or a true inability to classify the condition is alluded to in that the specific cause of death is reported to be of unspecified type.

The second example illustrates a patient who had six consultant episodes over a four month period during which time the patient was transfused with 17 units of red blood cells. The diagnosis reported during the first four consultant episodes was classified in this study as "myelodysplastic syndromes or polycythaemia vera", the pre-malignant haematological conditions. The diagnosis changed to leukaemia in the final two consultant episodes and the cause of death recorded one month later was unspecified myelodysplastic syndrome. Myelodysplastic syndromes (at one time referred to clinically as preleukaemia) variably transforms and progresses to acute myeloid leukaemia, thus the changing diagnoses reported in SMR01 records are likely to be reasonable.

Finally, the third example is of a patient who had several consultant episodes throughout the course of almost eight months ending with the death of the patient. In the first ten consultant episodes the recorded diagnosis was classified as myeloma, in the eleventh and final consultant episode the diagnosis was reported as lymphoma and the cause of death was recorded as plasma cell leukaemia. The changes in diagnoses are clinically intuitive as plasma cell leukaemia is related to multiple myeloma, another form of cancer that affects plasma cells: approximately one in 50 myeloma patients will eventually develop a leukaemia transformation (Leukaemia Research Foundation, online).

Figure 9.1 Examples of patient with more than one type of haematological condition

Example a.

Units used	Date of admission	Date of Discharge	Haematological diagnosis
5 RBC	02 June 2000	10 June 2000	Lymphoma
2 RBC	20 June 2000	21 June 2000	Lymphoma
4 RBC	27 June 2000	29 June 2000	Lymphoma
.	06 July 2000	16 July 2000	Leukaemia
Date and cause of death		16 July 2000	Peripheral & cutaneous T-cell lymphomas, unspecified

Example b.

Units used	Date of admission	Date of Discharge	Haematological diagnosis
3 RBC	12 January 2000	21 January 2000	MDS/PCV
4 RBC	03 February 2000	04 February 2000	MDS/PCV
3 RBC	02 March 2000	04 March 2000	MDS/PCV
3 RBC	20 March 2000	21 March 2000	MDS/PCV
.	04 April 2000	13 May 2000	Leukaemia
4 RBC	11 April 2000	14 April 2000	Leukaemia
Date and cause of death		13 May 2000	Acute myeloid leukaemia

Example c.

Units used	Date of admission	Date of Discharge	Haematological diagnosis
4 RBC	06 March 2000	08 March 2000	Myeloma
.	08 March 2000	31 March 2000	Myeloma
.	06 April 2000	11 April 2000	Myeloma
3 RBC	16 April 2000	19 April 2000	Myeloma
.	20 April	02 May 2000	Myeloma
.	23 May 2000	23 May 2000	Myeloma
.	29 June 2000	29 June 2000	Myeloma
.	24 July 2000	27 July 2000	Myeloma
3 RBC	29 July 2000	10 August 2000	Myeloma
4 RBC	25 September 2000	03 October 2000	Myeloma
.	17 October 2000	30 October 2000	Lymphoma
Date and cause of death		30 October 2000	Plasma cell leukaemia

The numbers of transfusion day records and SMR01-CD records that were linked to patients with more than one type of haematological condition diagnosed during the study are reported by first diagnosis (Table 9.5) and by combination of diagnoses (Table 9.6). If reported by first diagnosis most patients (16 out of 33) are classified in the myelodysplastic syndromes or polycythaemia vera case group (MDS/PCV). The findings indicate that all types of haematological condition defined here are found to be diagnosed in combination with MDS/PCV, the most common combination of case groups being leukaemia and MDS/PCV. Further, these findings support the descriptive investigations of SMR01-CD records described here (Figure 9.1). These combinations of diagnoses are considered to be reasonable given that MDS and PCV are pre-malignant conditions. However, the data does suggest that to classify patients by their first haematological diagnosis during the study will potentially overestimate blood use for MDS/PCV conditions and underestimate for the other conditions where a subsequent diagnosis of lymphoma, myeloma or leukaemia is made.

The small number of patients who were diagnosed with more than one type of haematological condition in the year 2000 represented a small amount of blood component use: 1.4% of red blood cell units, 2.0% of platelet units, 1.2% of FFP units and 0.7% of cryoprecipitate units that were attributed overall to haematological conditions. The findings for blood component use by first diagnosis and by combination of haematological diagnoses are reported in Tables 9.7 and 9.8.

Table 9.7 Blood component use for patients with more than one type of haematological condition diagnosed: by patients' first recorded diagnosis

Diagnosis	RBC units n=399	PLT units n=131	FFP units n=0	CRY units n=0	All units n=530
Lymphoma	107	23	0	0	130
Myeloma	24	0	0	0	24
Leukaemia	44	28	0	0	72
MDS/PCV	224	80	0	0	304

Table 9.8 **Blood component use for patients with more than one type of haematological condition diagnosed: by combination of diagnosis**

Diagnosis combinations *	RBC units n=399	PLT units n=131	FFP units n=0	CRY units n=0	All units n=530
Leukaemia & Myeloma	30	2	0	0	32
Lymphoma & Leukaemia	49	27	0	0	76
Lymphoma & MDS/PCV	60	7	0	0	67
Myeloma & MDS/PCV	10	0	0	0	10
Leukaemia & MDS/PCV	250	95	0	0	345

* Order reported in table does not reflect order in SMR01-CD records i.e. leukaemia & myeloma does not relate only to situations where leukaemia is the diagnosis made before myeloma, rather includes all instances of leukaemia & myeloma or myeloma & leukaemia combined diagnoses.

9.4. Overview of results for attribution of blood to Haematological case groups

This chapter reports on blood use for a small group of haematological diagnoses that were identified as representing the underlying clinical reason to explain why the patient was transfused, irrespective of other diagnoses and surgical procedures, because they are chronic diseases of the blood and blood forming organs for which blood transfusion is a usual treatment. The diagnostic blood attribution rule devised for the study states that all units of red blood cells transfused to a patient in the one year study period be attributed to the haematological diagnosis if the patient had a clinical coding of a diagnoses of malignant neoplasm of lymphoid or haematopoietic tissue, myelodysplastic syndromes or polycythaemia vera at any time during the study period. If a patient was diagnosed with more than one type of haematological condition blood use was attributed to the first such diagnosis in the patient's SMR01-CD records for the study period. Instances in which a patient had more than one type of haematological diagnosis were assessed separately but account for a small percentage of all red blood cell units used by haematological patients.

Figure 9.2 illustrates the overall distribution of the 7,286 red blood cell units (12.1% of total red blood cell units in the study) used by the 726 patients diagnosed with haematological conditions in the study population. Further, 47.8% of all platelet units, and 2.8% of all combined fresh frozen plasma and cryoprecipitate units, were transfused to these patients (Figure 9.3).

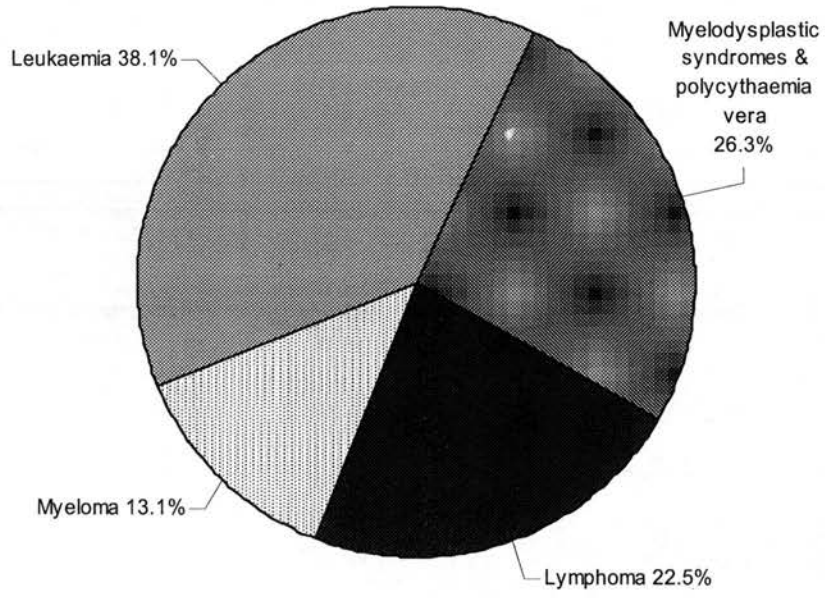
Examination of combinations of haematological diagnoses demonstrated that many instances were explained by the diagnosis of pre-malignant MDS/PCV conditions in combination with subsequent diagnoses of lymphoma, myeloma and leukaemia malignancies. This issue raises again the question as to what ought to be considered as the underlying reason for transfusion. It could be argued equally for haematological conditions that the use of blood results from either the treatment for the initial condition or for subsequent related or supplementary conditions, and even related procedures. However, because the number of patients implicated is very small and because the combinations of haematological conditions largely represent clinical progression of disease or similar underlying clinical requirements, the decision for the purposes of this study to attribute

blood use to the first occurring haematological diagnosis, echoing the rule for resolution of competing red cell using procedures, was validated.

In the study denominator data there were 1,061 patients (0.06% of the denominator population) with SMR01-CD records that contained a haematological diagnosis, as defined in this chapter. The study dataset contains transfusion data for 726 haematological patients: that is, approximately 68.4% of haematology patients in the study were transfused. In the data for all of Scotland for 2000 there were 4,686 patients (0.1% of the total Scottish population) with SMR01-CD records that contained a haematological diagnosis, a slightly higher proportion of haematology patients in the population than was described for the study denominator population. This can be explained because, in terms of haematology patients particularly, the study data is not representative of the whole of Scotland: in the east of Scotland one of the major centres for cancer patients is the Western General Hospital (WGH), Edinburgh, data for which is not included in this study. In the WGH alone, in 2000, there were 622 patients (13% of all haematological patients identified in all Scotland SMR01-CD records for 2000).

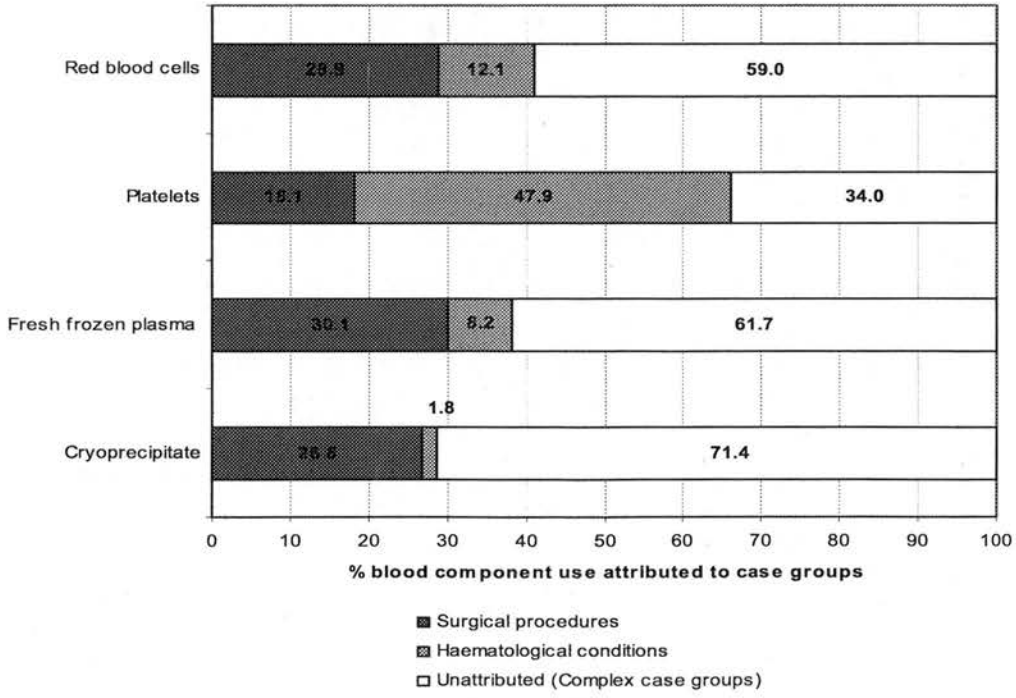
Furthermore, it was also possible to use the study dataset to quantify the overlap between surgical and haematological blood use. That is, for patients with diagnoses of haematological conditions during the study period, the amount of blood that could also be linked to surgical procedures they may also have had during the study period was quantified. The overlap of used units was small: 0.2% of red blood cell units, 0.3% of platelet units, and 0.1% of combined fresh frozen plasma and cryoprecipitate units could be attributed to both surgical events and haematological diagnoses. Figure 9.3 shows the distribution of used units of each blood component between the surgical and haematological case groups, and illustrates for the first time the remainder of used blood component units in the study dataset that are not attributable to either of the two clinical case groups defined for the study. The remaining units represent the future stages of analysis of the study dataset for which new clinical case groups will have to be defined and new approaches considered; opportunities that are discussed further in section 11.4

Figure 9.2 **Red blood cell units used by haematological condition calculated according to the diagnostic blood attribution rule**



n=7,286 red blood cell units

Figure 9.3 **Classification of blood component use to specified clinical case groups**



10. RESULTS: APPLICATIONS USING STUDY DATASET IN ANALYSES OF BLOOD COMPONENT USE

10.1. OVERVIEW OF ADDITIONAL APPLICATIONS USING STUDY DATASET

The results presented thus far have demonstrated that it is possible to link records from routine datasets and to use the data to describe blood use for well-defined clinical case groups. Further, the study dataset can be used to investigate a range of scenarios relating to the use of blood. The areas investigated here are:

- Best practice indicator: Total hip replacement surgery (section 10.2)
- Intra-operative cell salvage: Primary CABG surgery (section 10.3)
- Changes to the demographics of the Scottish population (section 10.4)
- Special interest case I: Thrombotic thrombocytopenic purpura (section 10.5)
- Special interest case II: Donor exposure (section 10.6)

10.2. BEST PRACTICE AND THE AGEING POPUALTION: TOTAL HIP REPLACEMENT SURGERY

10.2.1. Introduction to total hip replacement surgery

This section reports on analyses of red blood cell use for total hip replacement procedures, modelled to reflect a hypothetical situation in which procedures were to be transfused in accordance with best practice. Total hip replacement procedures were selected because they are commonly performed and are notable users of blood, as substantiated by findings reported for the surgical blood attribution rule (Chapter 8). Further, this modelling analysis is pertinent since both primary and revision hip replacement procedures are likely to become more common as the population ages.

Hip replacements involve the artificial replacement of inflamed and degenerating cartilage and bone of hip joints such as results from osteoarthritis and rheumatoid arthritis, and may also be used to repair hip fractures commonly caused by falls, particularly in old age when the bone is more brittle. These conditions cause chronic pain and reduced mobility. Primary hip replacements are successful and frequently performed procedures but eventually the replacement will fail because the materials wear out or because the artificial replacement is otherwise loosened, for example due to infection (National Audit Office, 2000). As a result revision hip replacements are necessary: these are usually more complex surgeries and are associated with higher failure rates. The number of primary and revision hip replacements being performed is rising as a direct consequence of the ageing population. More primary hip replacement procedures are required because people are living longer and more people are affected by typical conditions of old age such as osteoarthritis, or suffer falls as a result of unsteadiness and restricted mobility. It follows that as people with hip replacements live longer there will also be a requirement for more revision hip replacement procedures.

10.2.2. Methods used to examine the use of a best practice indicator in total hip replacement surgery

The analyses carried out for this study explored primary and revision total hip replacement procedures (OPCS-4 codes W37-W39), for which red blood cell use was described previously for the study data (section 8.4, Table 8.5). To explore the effect of changing practice to remove practice variation between hospitals, a series of best practice figures for red blood cell use per procedure performed were applied to a model of blood use for total hip replacement procedures across Scotland (Table 10.1). The number of procedures performed is the number of SMR01-CD records in which the procedure is coded in any procedural variable; an SMR01-CD record is counted once, irrespective of whether there is more than one primary or revision total hip replacement recorded during the same episode.

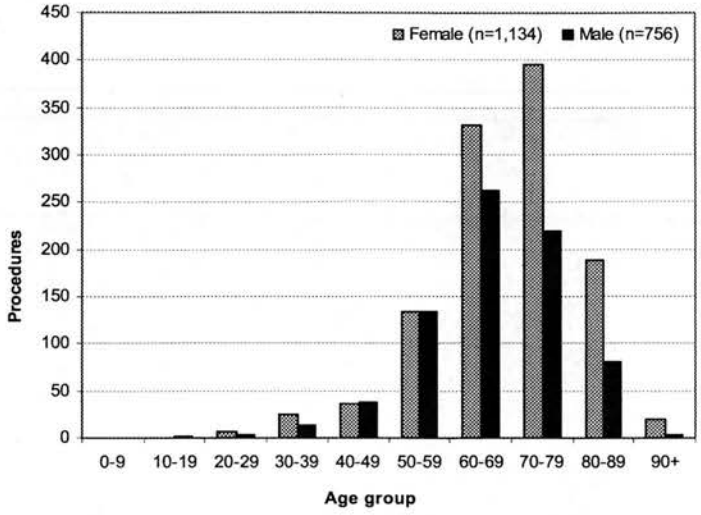
10.2.3. Results for the use of a best practice indicator in total hip replacement surgery

The total number of primary and revision total hip replacement procedures performed in the year 2000 for the denominator population for the study dataset was 1,890 (1,803 patients): 1,725 patients had one procedure, 72 patients had two procedures, three patients had three procedures and three patients had four procedures. The age and gender distribution of total hip replacement procedures for the study population is reported in Figure 10.1 which clearly illustrates that these are procedures associated with older age, and that in absolute numbers more females than males have hip replacements.

In the study dataset 1,034 transfusion day records accounting for 2,499 red blood cell units used could be attributed to 838 patients who had at least one transfused primary or revision total hip replacements. These 838 patients underwent a total of 895 primary or revision total hip replacement procedures during the year 2000. However, due to the structure of the dataset and the way calculations were made it is not possible to identify in an automated way for individual patients, the exact primary or revision total hip replacement procedure(s) transfused if patients had more than one procedure in the study to which a single transfusion event could be attributed to: calculations can be made manually or with

additional programming beyond the scope of this study. Therefore, data is described with respect to all procedures performed rather than procedures transfused (Table 10.1).

Figure 10.1 **Total hip replacement procedures for study denominator population by age and gender**



Based on 838 patients transfused and 1,803 patients operated, in the study at least 46% of primary or revision total hip replacements that were performed were transfused. The average number of red blood cell units used per procedure transfused was estimated to be 2.9 and the average number of red blood cell units used per procedure performed was 1.3. In the whole of Scotland for the year ending 31 March 2001 the number of primary and revision total hip replacement procedures performed was 5,127 (ISD, online). If it is assumed that these were transfused at the same rate as was determined for this study (1.3) then the national red blood cell use for primary or revision total hip replacements would have been 6,665 units.

Table 10.1 **Red blood cell use for primary and revision total hip replacement procedures: study data and estimates for all Scotland**

Population	TDR (RBC use)	RBC units used	Patients operated	Procedures performed	RBC/ Procedures performed
Study population	1,034	2,499	1,803	1,890	*1.3*
All Scotland	*2,758*	*6,665*	*4,978*	5,127†	***1.3***

Note1: Figures in italics are estimates calculated from the known data. Figure in bold italics is study rate applied to model. † ISD, online

Table 10.2 Red blood cell use per total hip replacement procedures by hospital

Hospital	Procedures performed n=1,890	RBC units used n=2,499	RBC/ Procedures performed
Raigmore	303	189	0.6
Woodend	564	1,222	2.2
Ninewells	157	302	1.9
Princess Margaret Rose	675	664	1.0
Edinburgh Royal Infirmary	86	56	0.7
Others*	105	66	1.6

* Hospitals where a small number of procedures performed: includes 5 procedures performed and 46 RBC units used at Aberdeen Royal Infirmary.

The findings reported in Table 10.2 are for variation in red blood cell use per total hip replacement procedure performed by hospital, within the study dataset: in this study red blood cell use per total hip replacement procedure performed ranged from 0.6 units to 2.2 units. By assuming that best practice is equivalent to the lowest rate observed in the study (0.6 RBC units per procedure performed), and by modelling this as the average rate of transfusion all total hip replacement procedures in Scotland in 2000, an estimated saving of 3,076 red blood cell units would be expected. This equates to a 53.8% saving in the number of red blood cell units used for all total hip replacement procedures in Scotland in 2000 compared to observed practice (Table 10.3). The amount of red blood cell units used for total hip replacements in Scotland in 2000 if a best practice indicator of 0.6 RBC units per procedure performed is applied is 2.1% of the estimated total red blood cell use for all Scotland in the year 2000.

The following examples model the effect of applying a best practice value that is not the lowest rate observed in the study but a similarly low value that could be considered to be an achievable rate for all hospitals. The hypothetical best practice example value of 1.0 red blood cell unit per procedure performed was applied to two models for the study data: firstly, to all hospitals in the study (23.1% saving in RBC use) and secondly, to only those hospitals with a higher observed practice and applying original, observed values to hospitals with a lower observed practice (29.1% saving in RBC use) (Table 10.3). In the first of these two models, the blanket rate of one red blood cell unit used per procedure performed for all

hospitals would reduce the number of units used by Woodend and Ninewells but would increase the number of units used by Raigmore and Edinburgh Royal Infirmary (Table 10.2). Thus it is most desirable to reduce the practice of the high users to meet best practice targets whilst encouraging previously low users to continue with current practice until further review of transfusion practices and guidelines is carried out.

Table 10.3 Potential savings in red blood cell use for total hip replacement procedures

Practice change	RBC/ Procedures performed	RBC units used	RBC units saved (%†)
Study (procedures performed = 1,890)			
Average rate across all hospitals	1.3*	2,457	.
Applying lowest rate across all hospitals	0.6	1,134	1,323 (53.8)
Applying example target rate across all hospitals	1.0	1,890	567 (23.1)
Applying example target rate by higher users & original rate by lower users	1.0	1,743	714 (29.1)
Scotland (procedures performed = 5,127)			
Average rate across all hospitals	1.3	6,665	.
Applying lowest rate across all hospitals	0.6	3,076	3,589 (53.8)
Applying example target rate across all hospitals	1.0	5,138	1,538 (23.1)

Note 1. "Others" (Table 10.2) considered as a single institution for purposes of these calculations. *2,499 RBC units/1,890 procedures = 1.32 RBC units per procedure performed, rounded to 1.3. † Saving relative to average rate of RBC units used per procedure performed across all hospitals = 2,457 RBC units used for Study and 6,665 for Scotland.

10.2.4. Overview of the use of a best practice indicator in total hip replacement surgery

While it might be thought that the best practice target rate of transfusion should be the lowest observed value, best practice targets are not simply about reducing blood use but also must take into consideration issues of clinical effectiveness and patient outcome. Using the data in this study 0.6 red blood cell units per procedure performed was the lowest reported rate but a target of, for example, 1.0 red blood cell units per procedure performed may be a more appropriate and achievable target for all hospitals, where supported by clinical evidence.

10.3. CONSIDERATION OF INTRA-OPERATIVE CELL SALVAGE IN CORONARY ARTERY BYPASS SURGERY

10.3.1. Introduction to coronary artery bypass graft surgery and intra-operative cell salvage

This section explores the impact of potential blood saving interventions on red blood cell use for a group of procedures that collectively represent high users of blood, coronary artery bypass grafts (CABG, OPCS-4 codes K40-46, Table 10.4). CABG procedures use grafts made from a healthy section of leg vein to bypass a damaged or diseased coronary artery, with the result of improving blood flow to the heart and reducing the chance of a heart attack. Coronary artery bypass graft procedures were included in the analysis of red blood cell use for surgical case groups (Chapter 8). The findings of those analyses revealed that CABG procedures used the highest proportion of red blood cell units that could be attributed to a surgical case group, 21.2% (primary and revision procedures combined). Because of their high demand for blood, CABG procedures are a good example for investigating the use of alternative techniques and interventions that have been suggested for reducing allogeneic blood use. Here the impact of applying a best practice model to red blood cell use in CABG surgery is compared with the potential savings that could be made using a mechanical intervention, intra-operative cell salvage (IOCS).

Table 10.4 Coronary artery bypass graft procedures included in analyses

OPCS-4 code	Coronary artery bypass graft procedure
K40	Saphenous vein graft replacement of coronary artery
K41	Other autograft replacement of coronary artery
K42	Allograft replacement of coronary artery
K43	Prosthetic replacement of coronary artery
K44	Other replacement of coronary artery
K442	Revision of replacement of coronary artery
K45	Connection of thoracic artery to coronary artery
K456	Revision of connection of thoracic artery to coronary artery
K46	Other bypass of coronary artery
K465	Revision of implantation of thoracic artery into heart

Intra-operative cell salvage enables blood that is recovered during surgery to be collected, processed and reinfused into the patient rather than being discarded as waste. In the processing stage the cell salvage device adds an anticoagulant in saline solution to the recovered blood which is then washed to remove byproducts and waste substances, and finally centrifuged to separate the red blood cells (McGill *et al*, 2002). Intra-operative cell salvage is increasingly endorsed for use in cardiothoracic and cardiovascular, as well as orthopaedic, surgeries for which the loss of blood is likely to be high (Carless *et al*, 2006). By reinfusing a patient with their own salvaged blood the risks associated with exposure to allogeneic transfusion and the pressure on donor resources can be reduced, although the risks associated with a new, mechanical intervention should also be considered. Because of this, of great interest is the potential savings in blood use due to intra-operative cell salvage.

10.3.2. Methods used to assess the use of intra-operative cell salvage in coronary artery bypass graft surgery

Red blood cell use for CABG procedures was analysed by hospital (Aberdeen Royal Infirmary and Edinburgh Royal Infirmary) to examine variation in practice. Figures for estimated savings achievable by using intra-operative cell salvage during CABG surgery were obtained from various sources and were applied to the data for the number of procedures performed and red blood cell units used per CABG procedure as determined for the whole Scottish population. The impact of intra-operative cell salvage on red blood cell use is compared with a best practice intervention for transfusion of coronary artery bypass graft procedures (Table 10.5).

10.3.3. Results for the use of intra-operative cell salvage in coronary artery bypass graft surgery

The use of red blood cells in CABG procedures for the study data is reported in Table 10.5. The majority of procedures were carried out in Aberdeen Royal Infirmary or Edinburgh Royal Infirmary. The findings for Aberdeen Royal Infirmary and Edinburgh Royal

Infirmary combined do not include two patients in the study data who underwent one CABG procedure each at Ninewells hospital, one of whom was transfused with four red blood cell units (the other was not transfused with red blood cell units). Therefore, in total 1,254 procedures performed of which 899 (71.7%) were transfused.

Each CABG patient underwent one CABG procedure and so the number of procedures equals the number of patients: with regards to processing, this meant that the complication of determining how many procedures were transfused for patients undergoing multiple procedures, as was encountered for total hip replacement procedures transfused (section 10.1), was not encountered in this analysis. Therefore, the number of *procedures performed* and the number of *procedures (patients) transfused* are reported in Table 10.6. Further, the following models in which best practice values and intra-operative cell salvage savings are applied are based on red blood cell units per *patient transfused* because that is the form in which values are expressed in previous studies. The number of *procedures performed* is calculated as any instance where a CABG procedure is coded in an SMR01-CD record, though the record is only counted once regardless of the number of CABG procedures coded in it. The number of *procedures transfused* is any instance where the CABG procedure is the first red cell using procedure coded in an SMR01-CD record that can be related by the surgical blood attribution rule to a transfusion day record of red blood cell use.

Table 10.5 Red blood cell use for Coronary artery bypass graft procedures: study data, showing variation by hospital, and estimates for all Scotland

Population	RBC units used	Procedures performed	Procedures transfused	RBC/ Procedures performed	RBC/ Procedures transfused
Aberdeen Royal Infirmary	637	443	206	*1.4*	*3.1*
Edinburgh Royal Infirmary	3,051	809	692	*3.8*	*4.4*
Study (ARI + ERI)*	3,688	1,252	898	*2.9*	*4.1*
All Scotland	*8,327‡*	2,832†	*2,031*	*2.9*	***4.1***

Note1: Figures in italics are estimates calculated from the known study data. Figure in bold italics is study rate applied to model. * Excludes 2 patients who underwent one CABG procedure each (total 2 procedures) at Ninewells hospital; transfusion data is available for one of these patients, who received 4 RBC units. ‡ Based on 4.1 RBC units / *procedure transfused* study figure. † Figure for year ending 31 March 2001 (ISD, online).

The total number of CABG procedures performed in the whole of Scotland (year ending 31 March 2001) was reported by ISD as 2,832 (ISD, online). Therefore, 44% of the CABG procedures performed in the whole of Scotland were included in the study data. It was expected that the study would represent approximately half of the CABG procedures performed in Scotland because the study data includes clinical and transfusion records for two (Aberdeen Royal Infirmary and Edinburgh Royal Infirmary) of the four main hospitals in Scotland where these procedures are performed. The remaining CABG procedures are performed in Glasgow Royal Infirmary and Glasgow Western Infirmary. The findings reveal differences between Aberdeen Royal Infirmary and Edinburgh Royal Infirmary in the number of units used per *procedure performed* (1.4 versus 3.8) and per *procedure transfused* (3.1 versus 4.4) (Table 10.5). Using the average number of red blood cell units used per *procedure performed* for the study data, 2.9, and making the assumption that the Glasgow hospitals transfuse CABG procedures at this average rate, the total red blood cell use estimated for the 1,578 CABG procedures performed in Glasgow is 4,576 units.

The average number of red blood cell units transfused per *procedure transfused* for the study data was 4.1: each patient had one CABG procedure and so the average number of red blood cell units transfused per *patient transfused* for the study data was also 4.1. Thus, a saving of 1.0 red blood cell unit per *patient transfused* could have been made if all CABG procedures performed in Scotland in the year 2000 had been transfused at the lower rate of Aberdeen Royal Infirmary (3.1 RBC units per *patient transfused*). At these rates the total red blood cell usage for total hip replacement operations in Scotland would have been 6,296 units; an estimated saving of 2,031 units (24.4% saving compared to study result of 8,327 RBC units) (Table 10.6).

Further, figures for potential savings made by using IOCS were obtained from a variety of sources. First, two studies of intra-operative cell salvage in cardiac surgery carried out ten years apart are described (Bell *et al*, 1992 and McGill *et al*, 2002). Bell *et al* described a median reduction of one unit of red blood cells in male patients, and two units in female patients undergoing first-time (primary) cardiac procedures who received intra-operative cell salvage compared to controls. However, there was no reduction in red blood cell use when all procedures were considered together (that is, including revisions) and there was no change in the number of other blood component units used. For the purposes of this

analysis the figure of 1.0 unit saved (best overall value) and 1.5 units saved (average of males and females) were modelled. McGill *et al* compared red blood cell transfusion between control patients, patients receiving intra-operative cell salvage, and patients receiving intra-operative cell salvage and acute normovolaemic haemodilution during elective CABG surgery. The study found that the proportion of patients transfused during CABG reduced from 51% in the control group to 31% in those patients who received intra-operative cell salvage (20% reduction in patients transfused), and the number of units used by transfused patients was reduced from 1.07 units per patient in the control group to 0.68 units per patient in the intra-operative cell salvage group (0.39 RBC units saved per patient) (McGill et al, 2002). Using these figures, the modelling analysis here demonstrates a total saving of 35.7% of red blood cell units (Table 0.6).

Table 10.6 Summary of red blood cell use for CABG procedures in Scotland based on best practice and intra-operative cell salvage figures

Intervention	RBC units saved/ Patient transfused	RBC units used/ Patient transfused	RBC units used	RBC units saved (%)*
Best practice				
As per Aberdeen Royal Infirmary	1.00	3.10	6,296	2,031 (24.4)
Intra-operative cell salvage				
Bell *et al*, 1992 I	1.00	3.10	6,296	2,031 (24.4)
Bell *et al*, 1992 II	1.50†	2.60	5,281	3,046 (36.6)
McGill *et al*, 2002 ‡	0.39	3.71	5,357‡	2,970 (35.7)
Carless *et al*, 2006	0.64	3.46	7,027	1,300 (15.6)

Note. Analyses based on 4.1 RBC units used/*patient transfused* and 2,031 patients transfused. * Percentage saving based on 8,327 units used for Scotland, 2000, estimated using 4.1 RBC units used per procedure transfused and 2,031 procedures transfused (Table 10.4.2). † Average of male (1.0) and female (2.0) savings reported in study. ‡ Based on 51% of patients (1,444) transfused i.e. 20% reduction in number of patients transfused.

A Cochrane review entitled "Cell salvage for minimising peri-operative allogeneic blood transfusion" was published in 2006 (Carless *et al*, 2006). The meta-analysis of controlled trials of intra-operative cell salvage in elective surgery gave an overall figure of 0.67 units (95% CI 0.45 to 0.89 units saved) for the savings made by using intra-operative cell salvage. 23 of the studies reviewed in the Cochrane report investigated cell salvage in cardiac surgery specifically: the reduction in blood use was 0.64 units (0.39 to 0.90 units saved) per patient.

A larger reduction was made in orthopaedic surgery specifically (0.89 units per patient; 95% CI 0.39 to 1.40 units saved), and no statistically significant reduction was observed in vascular surgery (0.02 units per patient; 95% CI 0.34 units saved to 0.38 units more required). The review also concluded that the methodology of studies included in the meta-analysis was poor and potentially biased in favour of cell salvage.

In this study all patients had one CABG procedure and so if the Cochrane review figures for *procedures transfused* are used as a proxy for the number of *patients transfused* and the value for a saving of 0.64 units per *patient transfused* is applied (Carless *et al*, 2006), 2,031 CABG patients would be transfused with an average of 3.46 units, which results in a total use of 7,027 red blood cell units, and gives a saving of 1,300 units (15.6%) by this model (Table 10.6).

10.3.4. Overview of the use of intra-operative cell salvage in coronary artery bypass graft surgery

The percentage savings reported for various estimates of red blood cell reductions using intra-operative cell salvage in CABG surgery described here ranges from 15.6% to 36.6%. These savings equate to between 1,300 units to 3,046 units, or 0.8% to 1.8% of the total red blood cell use in Scotland for the year 2000 estimated in this study. The smallest and greatest savings were achieved using the figures that estimate the impact of intra-operative cell salvage; applying a best practice model based on the number of units transfused by Aberdeen Royal Infirmary in the year 2000 gives a result that lies in the middle of the range and is equal to one of the intra-operative cell salvage estimates.

The evidence suggests that the use of intra-operative cell salvage in CABG procedures can achieve notable savings in allogeneic red blood cell use for these procedures, but equally, changing practice could have comparable savings. Furthermore, by reducing allogeneic transfusion, recipients' donor exposure and hence the risk of transfusion-transmitted infection are reduced, and red blood cell stocks are conserved.

10.4. CHANGES TO DEMOGRAPHICS OF THE SCOTTISH POPULATION

10.4.1. Introduction to demographic change in Scotland

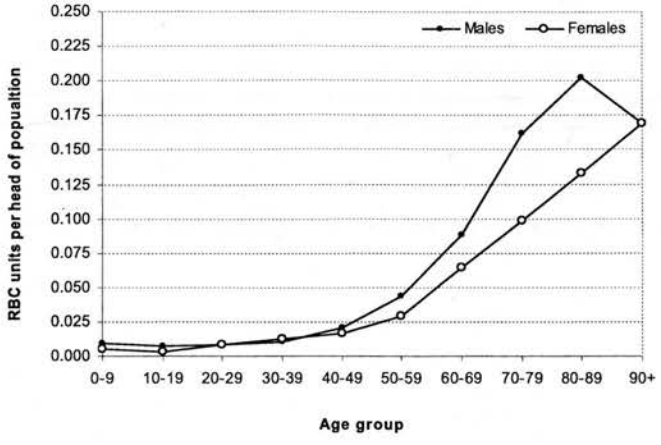
Variations in blood component use by age group and gender were described in Chapter 7. In particular the findings showed that older age groups (over 60 years of age) receive the highest number of red blood cell units per patient. Population projections show that Scotland has an ageing population that is characterised by significant increase in the older age groups (GRO, online; ESRC, 2004). Given the high rate of transfusion in older patients the future impact of an ageing population on red blood cell use in Scotland is explored. The effect of the ageing population makes it particularly important to monitor blood use for total hip replacement procedures given that they are most commonly performed for patients over 60 years of age.

10.4.2. Method used to assess impact of demographic change on blood use

Red blood cell use, as observed in the study dataset, was applied to revised mid-year population estimates for years 2000 (published in July 2007), accounting for the proportion of the population that was transfused, to determine rates of red blood cell use for the Scottish population in the year 2000, separately for each ten year age group and for males and females. These rates show an increase in units used per head of population with advancing age (Figure 10.3). A comparison was made of projected and revised mid-year population estimates for the Scottish population in 2000 (GRO, online). There was little difference between the overall predicted and actual population figures, though there was some variation by age group. The predicted population had overestimated the number of males aged 80-89, and underestimated for age groups 0-9, 20-29, and 90 plus for both sexes. Thus, the analyses reported here were carried out using the revised mid-year population estimates for 2000. The above comparison alerts to potential errors in the projections for the 2016 and 2031 populations. Indeed GRO are careful to highlight the uncertainty in

projections due to unpredicted changes in demographic trends, and this should be considered when interpreting the findings of this study.

Figure 10.3 Red cell units used per head of population (based on study data)

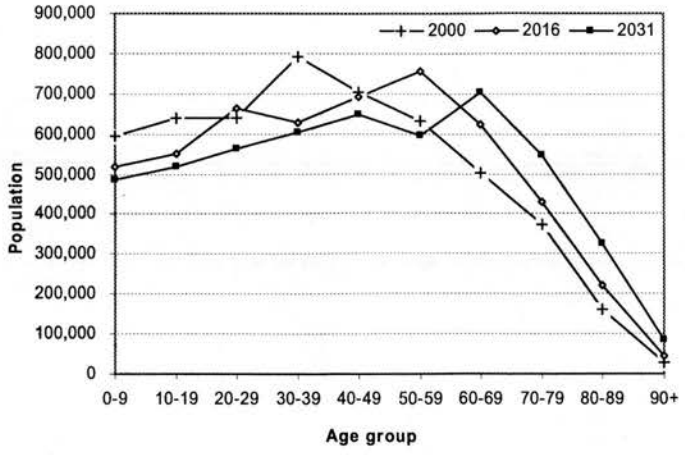


The age and gender specific rates of red blood cell use for the Scottish population in the year 2000 (Figure 10.3) were then applied to projected population estimates for 2016 and 2031 (based on predicted 2004 data) (GRO Scotland, online). The year 2031 was chosen because it is the furthest forward for which the GRO Scotland has made population projections at this time; 2016 is included as a mid-way reference point. The 2016 and 2031 projections provide population figures for estimating changes in blood use assuming that the pattern of blood use within age groups is unchanged, that is, assuming that the clinical indications for which blood is used, and/or transfusion practice with respect to blood use for these indications, is unchanged.

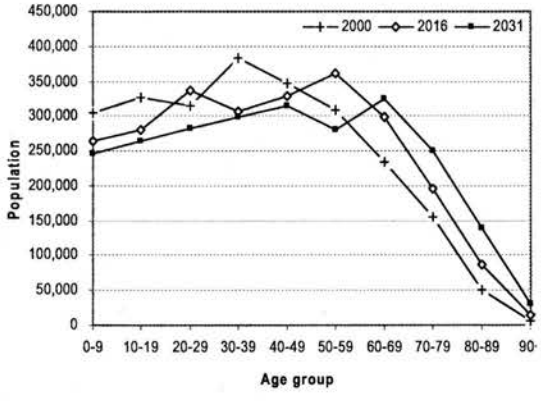
The population figures for the three years, 2000, 2016 and 2031 for the total population and separately for males and females are shown (Figure 10.4a-c). The population data shows a marked decrease in the size of the younger age groups over the period 2000 to 2031, and a marked increase in the older age groups over the years from 2000 to 2031. The particular increase in the number of older males also causes a gender effect: between 2000 and 2016 red blood cell use is predicated to increase by 23.7% for males compared with 13.4% for females (17.4% overall increase in RBC units used).

Figure 10.4a-c Population estimates for all Scotland for years 2000, 2016 and 2031

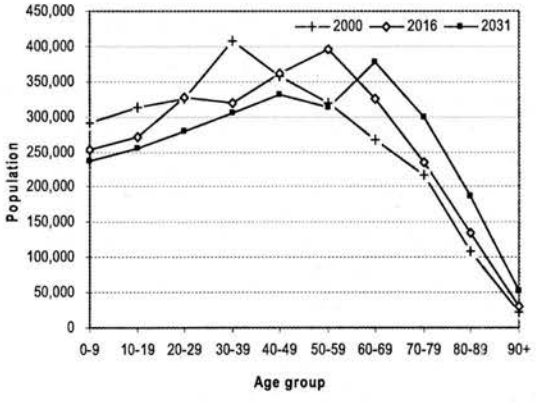
a. All persons



b. Males



c. Females



To assess the effect of the changing population demographics in Scotland on the use of blood for hip replacements, the age and gender specific use of red blood cell units per procedures performed per head of population obtained from the study's denominator data were applied to the projected population structure for the year 2031. Red blood cell use was calculated based on the best practice figure obtained from analyses above and the analysis carried out for primary and revision procedures separately.

10.4.3. Results for impact of demographic change on blood use

Red blood cell use is predicted to decline in the younger age groups, but there is a larger predicted increase in the use of blood by the older age groups (over 60 years), particularly for males, reflecting the population expansion in these age groups (Figures 10.5a & 10.5b). The estimated number of red blood cell units used in the whole of Scotland in 2000 was 158,863 (70% of RBC units supplied, section 6.1.2). The absolute figures for red blood cell use in 2000, 2016 and 2031 are shown (Figure 10.6). Overall, between 2000 and 2016 there is a predicted increase in red blood cell use of 17.4% (approximately an additional 28,000 RBC units), and between 2016 and 2031 a further increase of 17.3% (approximately an additional 32,000 RBC units).

Figure 10.5a Estimated red blood cell use for Scotland in 2000, 2016 and 2031 by age

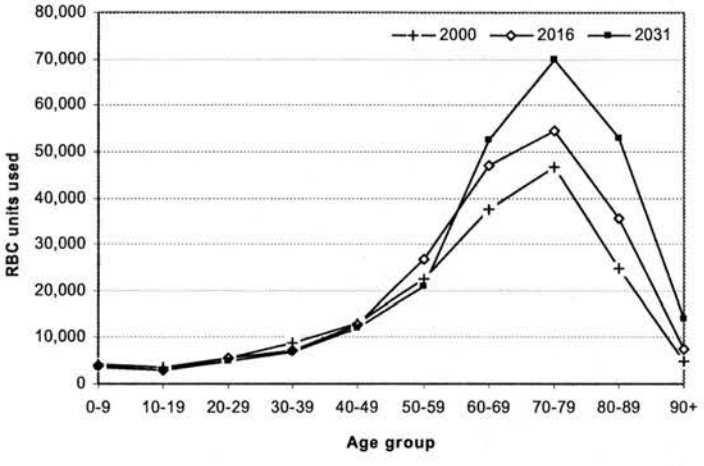


Figure 10.5b Detailed view showing reduction in use for age groups 0-9 to 40-49 years

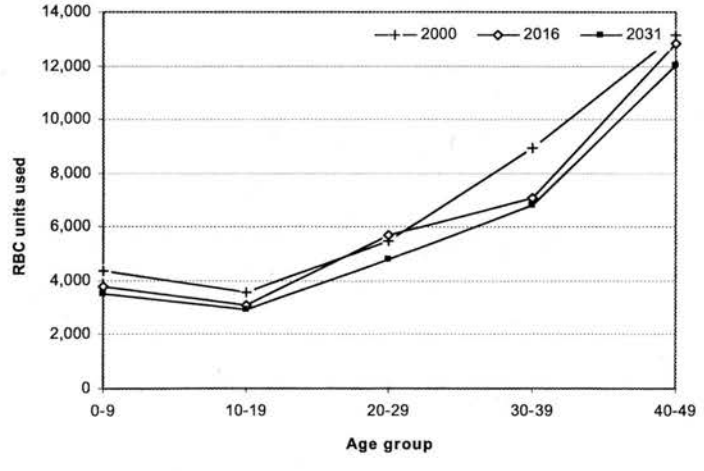
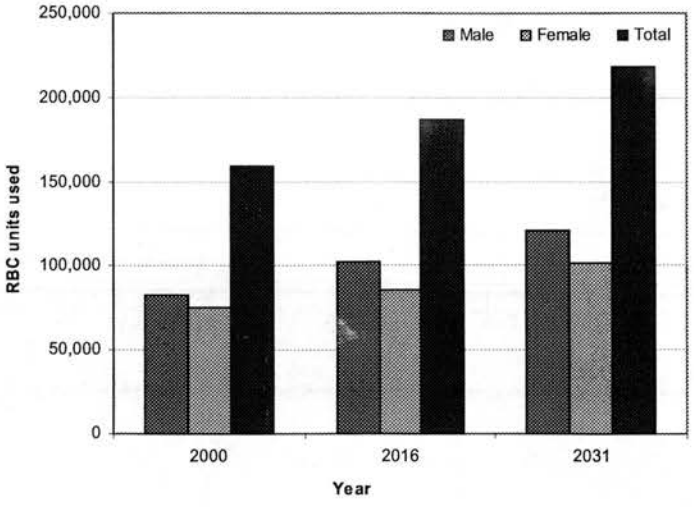


Figure 10.6 Red blood cell use in 2000, 2016 and 2031 by gender



Considering the population data and projected red blood cell use figures together reveals that between 2000 and 2016 a 1.3% growth in the size of the population is matched by a 17.4% increase in red blood cell use. Between 2016 and 2031 the population is estimated to decrease by 1.2% (0.08% per year) and red blood cell use is estimated to increase by 17.9% (1.2% per year). Although the overall size of the population in 2000 and 2031 is predicted to be approximately the same it is estimated that 37.8% more red blood cell units (approximately an additional 60,000 RBC units overall) will be used in 2031 than were used in 2000 if current patterns of usage are maintained.

One surgical procedure that is most common in the elderly is total hip replacement. This has already been considered in terms of savings that could be made by encouraging orthopaedic surgeons to agree and utilise a best practice target value for the use of blood for total hip replacement surgery (section 10.1). Further to analysis of best practice, the effect of the ageing Scottish population on the use of red blood cell units between 2000 and 2031 for total hip replacements was assessed here. The estimated number of red blood cell units used for all total hip replacement procedures in 2031 was 27,250, which equates to 11.5% of the estimated total red blood cell use for Scotland in that year, and an estimated increase in the use of red blood cells for total hip replacement procedures of 30.5% between years 2000 and 2031 (Table 10.7). The percentage change in red blood cell use between 2000 and 2031 is greater for revision procedures than primary procedures. Further, for revision procedures

the change in use is greater in males than in females, which echoes the greater population expansion of older males compared with females. For primary procedures the change in use for males and females is roughly equal, though slightly greater for females.

Table 10.7 Estimated red blood cell units used in 2031 and percentage change between 2000 and 2031 for total hip replacements for whole of Scotland

Type of THR procedure	RBC units used			% change in RBC use (2000 to 2031)		
	Male	Female	All persons	Male	Female	All persons
Primary THR	9,113	14,733	23,846	28.1	30.4	29.5
Revision THR	1,497	1,906	3,403	47.0	31.5	37.9
All THR procedures	**10,610**	**16,639**	**27,249**	**30.5**	**30.5**	**30.5**

* THR: Total hip replacement

10.4.4. Overview of impact of demographic change on blood use

The findings indicate that large increases in red blood cell use in Scotland are accounted for by the expanding population in the older age groups (typically over age 60 years) for whom the use of red blood cell units per patient is higher than for other age groups. Concurrently, the population and total red blood cell units used by the under 60s is predicted to decline; the decline in the size of the population in the younger age groups will also affect the donor population and hence add to pressures working to reduce the supply of blood.

The saving in red blood cell use for total hip replacement procedures that could be achieved with best practice targets was estimated to be as much as 23%; and perhaps even as high as 54% if all hospitals in Scotland transfused total hip replacement procedures at the lowest rate observed for this study (section 10.1). Thus, the anticipated increase in red blood cell use due to the ageing population, and specifically for total hip replacement procedures could be negated by considering the use of blood conservation strategies, such as applying best practice targets, in the future.

The projections reported here were made on the assumption that the pattern of red cell use by age will remain the same. However, it should be emphasised that the use of blood is

influenced by the epidemiology of disease, by changes to clinical practice and treatment protocols, and by changes in transfusion practice including the use of new and alternative techniques and interventions. Where appropriate estimates for these changes are available, alternative models of future blood use could be made to account for such factors.

10.5. SPECIAL INTEREST CASE I: THROMBOTIC THROMBOCYTOPENIC PURPURA

10.5.1. Introduction to Thrombotic thrombocytopenic purpura

This section describes the use of the data in examining the use of blood components for a medical condition known to have a very low incidence but a very high associated use of blood components, specifically fresh frozen plasma. Thrombotic thrombocytopenic purpura (TTP) is a rare condition in which there is deficiency in the function of an enzyme (ADMS-2) that cleaves von Willebrand factor resulting in the inappropriate formation of platelet clumps. The deficiency may be inherited and therefore symptomatic in childhood (extremely rare) or it can be acquired later in life (1-3 cases per million per year; approximately 5-15 cases in Scotland). Patients suffer complex disturbances of haemostasis and haemolysis of red blood cells (Pisoni & Remuzzi, 2000).

The treatment for TTP involves repeated plasma exchanges in which patients' plasma is replaced with donor fresh frozen plasma (FFP). Each treatment involves the use of about five litres of fresh frozen plasma and patients may require serial courses of treatment each lasting five days (one exchange per day). One unit of FFP is 0.25 litres, therefore 20 units of FFP are given in each exchange and in total 100 units of FFP are required for every five day treatment course. Recent evidence questions the general prophylactic use of FFP and proposes that TTP is the only condition for which there is evidence that treatment using FFP transfusion is effective (Stanworth *et al*, 2004).

There is currently no specific, routine test for TTP and instead the diagnosis is made on the basis of symptoms and tests for non-specific markers in blood. Further, there is no specific ICD-10 code for recording a diagnosis of TTP in clinical records. TTP would be expected to fall under ICD-10 section "D69: Purpura and other haemorrhagic conditions" (Table 10.8); it may also be coded as a thrombotic microangiopathy (ICD-10 code "M311"), a term that describes syndromes caused by impaired platelet aggregation, including thrombotic thrombocytopenic purpura and haemolytic uremic syndrome (Pisoni & Remuzzi, 2000).

Table 10.8 D69 sub-chapter of ICD-10: Purpura and other haemorrhagic conditions

ICD -10 code	Purpura and other haemorrhagic conditions
D690	Allergic purpura
D691	Qualitative platelet defects
D692	Other non-thrombocytopenic purpura
D693	Idiopathic thrombocytopenic purpura
D694	Other primary thrombocytopenia
D695	Secondary thrombocytopenia
D696	Thrombocytopenia, unspecified
D698	Other specified haemorrhagic conditions
D699	Haemorrhagic condition, unspecified

10.5.2. Methods used to examine fresh frozen plasma use by patients with Thrombotic thrombocytopenic purpura

Because of the lack of specific clinical coding and because the condition requires treatment consisting of high use of FFP, a D69 code in combination with a large number of FFP units used may be indicative of a diagnosis of thrombotic thrombocytopenia purpura. For this analysis, patients with any coding of D69 in SMR01-CD records were selected and their FFP use and additional clinical data were examined. Further, because the condition was not well characterised or recognised at the time (2000), other diagnostic information in the clinical records of FFP users was considered for its ability to identify of potential or probable TTP patients. This step helped to identify thrombotic microangiopathy as an indicator for thrombotic thrombocytopenia purpura and so the FFP use of patients with any coding of M311 in the diagnostic variables of SMR01-CD records was also examined.

Therefore, evidence of the indicators "D69" and "M311" coding, and FFP high use in the study dataset was examined to identify TTP patients. Groups defined by each of these indicators are described separately first, following which, patients common to two or more groups are summarised. Once identified, the FFP use of these patients was quantified to identify the proportion of all FFP units used in the study that could be attributed to this condition for which there is recent evidence to suggest it as the only condition that can be effectively treated with FFP transfusion.

10.5.3. Results for fresh frozen plasma use by patients with Thrombotic thrombocytopenic purpura

In the study dataset 171 patients with a D69 code in any diagnosis (ICD-10) variable were linked to transfusion day records of blood component use. The total number of SMR01-CD records for these patients was 459. Specifically, 25 patients with a D69 coding (55.6% male, mean age 53.8 years (s.d. 11.87 years, range 26-88.3 years)) could be related to 72 transfusion day records (471 units) of FFP use. A summary of D69 codes and FFP use by patient is given: two patients who were transfused with a large number of FFP units in comparison with the others in this group can be identified (patients 12 and 16, Table 10.9).

Table 10.9 Patients with SMR01 records in which there is a D69 code: breakdown of D69 codes and total FFP use

Patient	SMR01 1*	SMR01 2	SMR01 3	SMR01 4	SMR01 5	Number of D69s	Total SMR01	FFP units used
1	D696	D695				2	29	16
2	D696	D696	D696			3	7	12
3	D696					1	3	6
4	D696	D696				2	8	2
5	D696	D696	D696			3	4	5
6	D696	D696				2	16	4
7	D696					1	2	2
8	D696	D696	D696	D696		4	4	6
9	D696					1	6	3
10	D696					1	1	3
11	D696					1	3	11
12	**D696**					**1**	**3**	**145**
13	D696	D696	D696	D694	D696	5	8	8
14	D696	D696				2	8	7
15	D696					1	13	7
16	**D694**	**D694**	**D694**			**3**	**7**	**197**
17	D696	D696				2	7	3
18	D696	D696				2	3	3
19	D696					1	2	2
20	D696	D696				2	8	4
21	D965					1	4	10
22	D696	D693				2	3	2
23	D696					1	1	6
24	D696					1	21	4
25	D696					1	1	3

* The SMR01 records in which D69 diagnoses were coded are not necessarily consecutive.

Table 10.10 Patients with more than 100 FFP units used in 2000

Patient	RBC units used	PLT units used	FFP units used	CRYO units used	Total units used
a	28	0	278	0	306
b	4	0	158	0	162
c	112	1	1,776	10	1,899
d	15	0	124	0	139
e	0	0	145	0	145
f	14	0	197	0	211

It was hypothesised that by examining the SMR01-CD records of patients transfused with more than 100 units of FFP during the study period, patients who, while not coded with a D69 diagnosis, but were coded with other diagnoses that are indicative of pre-thrombotic thrombocytopenia purpura conditions such as haemolytic disease (which can be caused by E-coli 0157 infection), renal failure (implicated in childhood cases of haemolytic uraemic syndrome) and neurological conditions, may be identified (Table 10.10). These patients include two (listed as patients "c" and "e") that were considered to be outliers in the analysis of FFP use by age and gender because of their high use of FFP units, and were subsequently removed from the data reported elsewhere (section 7.4.2). A third patient also considered to be an outlier in section 7.4.2 was transfused with 76 units of FFP: the primary diagnosis in the patient's first SMR01-CD record in the study dataset was chronic renal failure, a condition linked with the development of thrombotic thrombocytopenia purpura. Given this diagnosis, and that the patient may have received additional FFP transfusions beyond the time-scale of this study, this patient could also be considered to be a potential TTP patient but does not meet the criteria required for this specific analysis. Similarly, patient "d" (Table 10.10) was transfused with 124 FFP units but could not be linked to a D69 or M311 diagnosis and so although the patient was diagnosed with nephrotic syndromes, indicative of renal disease, they too are excluded from this specific analysis. Patient "f" was transfused with 197 FFP units and although the *principal* diagnoses (reported in Table 10.5.4) do not contain a TTP-related condition, the patient was diagnosed with E-coli infection and has D694 and D593 (haemolytic-uraemic syndrome) codes recorded in the fourth and third diagnoses variables of three SMR01-CD records. Thus, patients "a-c" and "e-f" do meet the selection criteria for this analysis.

Table 10.11 Summary of primary diagnosis of patients transfused with more than 100 units of FFP during the study period

Patient*	FFP units used	Date of Admission	Date of Discharge	Primary diagnosis
a	278	25.9.00	27.9.00	Haemolytic-uraemic syndrome
		27.9.00	28.9.00	Haemolytic-uraemic syndrome
		28.9.00	6.10.00	Thrombotic microangiopathy
		6.10.00	7.11.00	Thrombotic microangiopathy
		23.11.00	1.12.00	Preparatory care for dialysis
		3.12.00	14.12.00	Chronic renal failure
		14.12.00	17.12.00	Chronic renal failure
		17.12.00	19.12.00	Chronic renal failure
b	158	8.10.00	12.10.00	Thrombotic microangiopathy
		12.10.00	26.10.00	Thrombotic microangiopathy
c	1,776	1.5.00	2.5.00	Fracture of vault of skull
		2.5.00	4.5.00	Thrombotic microangiopathy
		4.5.00	7.5.00	Pneumonia, unspecified
		7.5.00	19.6.00	Thrombotic microangiopathy
		19.6.00	19.6.00	Other and unspecified intestinal obstruction
		19.6.00	20.6.00	Thrombotic microangiopathy
		20.6.00	4.7.00	Thrombotic microangiopathy
		4.7.00	11.9.00	Thrombotic microangiopathy
		11.9.00	20.9.00	Thrombotic microangiopathy
		20.9.00	8.10.00	Thrombotic microangiopathy
		8.10.00	9.10.00	Other and unspecified intestinal obstruction
		11.10.00	14.10.00	Thrombotic microangiopathy
		14.10.00	16.10.00	Other specified disorders of thyroid
d	124	15.9.00	21.9.00	Nephrotic syndrome
		21.9.00	26.9.00	Nephrotic syndrome
		1.11.00	8.11.00	Nephrotic syndrome
		10.12.00	11.12.00	Nepthrotic syndrome
		11.12.00	13.12.00	Focal and segmental glomerular lesions
		13.12.00	19.12.00	Respiratory failure
		19.12.00	22.12.00	Focal and segmental glomerular lesions
		22.12.00	28.12.00	Unspecified acute lower respiratory infection
e	145	29.12.99	1.1.00	Thrombocytopenia, unspecified
		11.1.00	11.1.00	Thrombotic microangiopathy
		28.2.00	28.2.00	Thrombotic microangiopathy
f	197	3.5.00	5.5.00	Anaemia
		5.5.00	14.5.00	Anaemia
		9.5.00	9.5.00	Anaemia
		19.6.00	21.6.00	Enterotoxigenic Escherichia coli infection
		21.6.00	22.6.00	Enterotoxigenic Escherichia coli infection
		22.6.00	29.6.00	Other bacterial infections of unspecified site
		29.6.00	14.7.00	Enterotoxigenic Escherichia coli infection

* Patients are the same patients as those included in Table 10.10

Patients with any diagnosis of thrombotic microangiopathy (M311) are summarised in Table 10.12; together they use 2,366 FFP units. The group includes one patient who was transfused with nine FFP units and who is therefore not considered to be a likely TTP patient. However, this patient was not transfused with more FFP units because they died, aged 95 years, just 13 days after the date of admission and first diagnosis of thrombotic microangiopathy.

Table 10.12 Patients with an M311 code in any ICD-10 field in 2000

Patient	Number of M311 codings	Total number of SMR01-CD records	FFP units used (n=2,366)
i	5	8	278
ii	2	2	158
iii	14	14	1,776
iv	2	3	145
v	1	2	9

10.5.4. Overview of fresh frozen plasma use by patients with Thrombotic thrombocytopenic purpura

The exploration of D69 coding (purpura and other haemorrhagic conditions), M311 (thrombotic microangiopathy) and high use of FFP (typically more than 100 units) in the study dataset, identified five patients (Table 10.13). In total these patients used 2,554 FFP units, 27.0% of all FFP units used in the study. With recent evidence suggesting that this is the only condition for which treatment with FFP is effective, there is potential for a 73.0% saving in FFP units if used only for treatment of the TTP-related conditions described here.

Table 10.13 Summary of D69 coding, M311 coding and FFP use (>100 units) in 2000

Patient	Number of D69 codings	Number of M311 codings	Total number of SMR01-CD records	FFP units used (n=2,554)
A *	0	5	8	278
B	0	2	2	158
C	0	14	14	1,776
D	1	2	3	145
E *	3	0	7	197

* Also have ICD-10 code for diagnosis of haemolytic-uraemic syndromes

10.6. SPECIAL INTEREST CASE II: DONOR EXPOSURE

10.6.1. Introduction to donor exposure

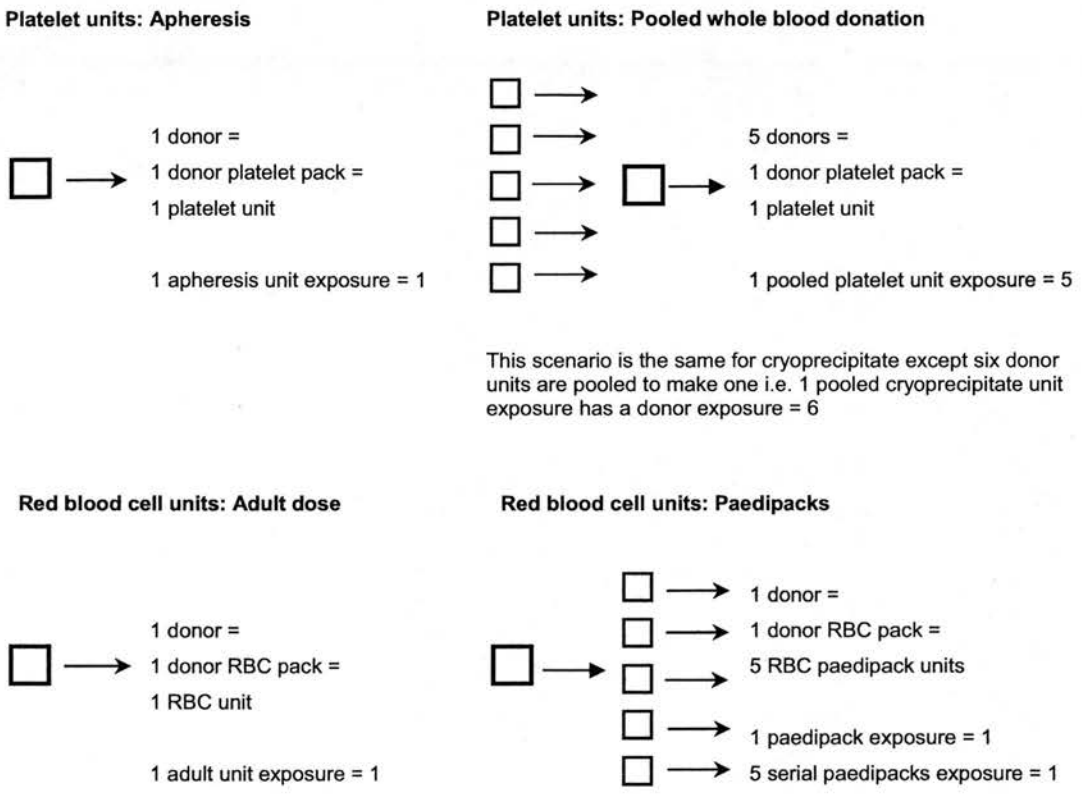
Donor exposure is a measure of the number of donors to whom blood recipients are exposed via blood transfusion over a specified time period (lifetime, for example). This is important when considering the combined risks of infection faced by patients throughout their lifetime, particularly so for patients who receive high numbers of transfused units. This section explores how the data can be used to calculate and describe donor exposure in the context of transfusion-transmissible infections. Thus, this section goes beyond describing the use of blood to examine one aspect of the impact of the use of blood on transfusion recipients.

Donor exposure is calculated from the total number of blood component units transfused to a recipient. A unit of red blood cells, a donation, is comprised of red blood cells from one blood donor given during a single donation. Thus for a patient transfused with one unit of red blood cells the donor exposure is one. The case is the same for fresh frozen plasma: one unit of FFP is the plasma obtained from a single unit of whole blood from a single donor and so the donor exposure is one.

However, the production and blood bank assignment processes are different in the cases of platelet, cryoprecipitate and paediatric red blood cell units. Platelet units are produced in one of two ways: platelet units are either obtained from a single donor by apheresis or are pooled from multiple whole blood donations. Apheresis is a process in which whole blood is removed from the donor, the required portion is separated off and the remaining components are transfused back into the donor. A unit of platelets obtained in this way comes from a single donor and has a donor exposure of one. However, an adult dose unit of pooled platelets is derived from multiple, usually five, different whole blood units because there is only a small volume of platelets in whole blood donations, insufficient to produce a whole unit. This means that a single unit of pooled platelets actually represents five donors and the donor exposure of pooled platelet recipients is five times higher than for platelet units produced by apheresis (Figure 10.2). In this study platelet units are adult dose equivalent units derived from pooling multiple (five) donations. Therefore, the number of

platelet units must be multiplied by five to quantify the actual donor exposure (Figure 10.7). Cryoprecipitate is also produced by pooling units from separate donations to produce an adult dose unit, in this case from six donors. Therefore, the number of cryoprecipitate units must be multiplied by six to get the correct measure of donor exposure presented by one cryoprecipitate unit.

Figure 10.7 Relationship between unit preparation and donor exposure



Red blood cells are transfused to paediatric patients in the form of "paedipacks". These are small volume donor packs produced by splitting a single adult red blood cell unit into five paedipacks thereby providing volumes suitable for transfusion to paediatric patients (Figure 10.2). Paedipacks were primarily developed to reduce the donor exposure of paediatric patients, who may require multiple transfusions and are especially vulnerable to infection risks, as well as to reduce wastage and aid transfusion of small volumes. Thus, a paediatric patient who receives one paedipack transfusion of red blood cells is exposed to a single

donor, and moreover, the donor exposure remains one for subsequent, serial transfusions with red blood cell paedipacks from the same original donor pack up to the transfusion of all five paedipacks. Only at the sixth transfusion does donor exposure increase to two.

A single adult red blood cell donor pack gives rise to five paedipacks that should be recorded individually by the blood bank as they are assigned. The proportion of red blood cell units assigned in the form of paedipacks is not given in the study's transfusion data and thus the magnitude of the overestimation of donor exposure for red blood cell units cannot be calculated. For the purposes of this study no adjustment was made to take into consideration the impact of paedipacks on donor exposure calculations i.e. all units of red blood cells were calculated as having a donor exposure of one.

10.6.2. Methods used to examine donor exposure

Donor exposure for patients in the study dataset was calculated using the multiplication factors illustrated in Table 10.14: red blood cells and FFP are multiplied by a factor of one, platelets by a factor of five and cryoprecipitate by a factor of six. The unadjusted and adjusted donor exposure figures are reported for all patients (Table 10.15). Furthermore, donor exposure and infection risks are considered together to describe the actual risk of infection to the patient (Table 10.16). In addition, adjusted donor exposure figures are reported for surviving and non-surviving patients according to date of death available at the time of data extraction in 2004 (Table 10.17).

Table 10.14 Examples of conversion of blood component units to donor exposure

Units (recorded in transfusion day record)					Donor exposure (after multiplication)				
RBC	PLT	FFP	CRYO	Total	RBC	PLT	FFP	CRYO	Total
1	.	.	.	**1**	1	.	.	.	**1**
.	1	.	.	**1**	.	5	.	.	**5**
.	.	1	.	**1**	.	.	1	.	**1**
.	.	.	1	**1**	.	.	.	6	**6**
1	1	.	.	**2**	1	5	.	.	**6**
1	1	1	.	**3**	1	5	1	.	**7**
1	1	1	1	**4**	1	5	1	6	**13**

10.6.3. Results of donor exposure analyses

Examples of the multiplications required to calculate patients' donor exposure are illustrated in Table 10.14. Even these simple examples illustrate the impact of multiple units of platelets or cryoprecipitate on patients' total donor exposure. A low level of red blood cell transfusion represents a low donor exposure but this can be particularly increased by the additional transfusion of even a small number of platelet or cryoprecipitate units. First, unadjusted and adjusted figures for total donor exposure in the year 2000 are compared for all patients in the study dataset (Table 10.15). It is acknowledged that the study data is representative of a single year and so the total donor exposure is the minimum exposure that these patients will experience in their lifetime. A proportion will have already been exposed to other transfusions prior to the start of the year 2000 and a proportion of the surviving patients will have gone on to have further transfusions after the end of the year 2000.

Table 10.15 Patients in study dataset grouped by total donor exposure: unadjusted and adjusted values

Total Donor Exposure in 2000	Patients (% all patients) (n=11,994)	
	Unadjusted*	Adjusted*
1-9	10,331 (86.1)	9,988 (83.3)
10-19	1,035 (8.6)	1,110 (9.3)
20-29	275 (2.3)	347 (2.9)
30-39	133 (1.1)	135 (1.1)
40-49	90 (0.8)	79 (0.7)
50-59	43 (0.4)	58 (0.5)
60-69	18 (0.2)	42 (0.4)
70-79	19 (0.2)	35 (0.3)
80+	50 (0.4)	200 (1.7)

*Unadjusted figures calculated from original data for units used; Adjusted figures account for platelet units x5 and cryoprecipitate units x6.

The proportion of all patients in the study dataset who had a donor exposure of less than ten blood component units in the year 2000 was 86.1% by the original, unadjusted data and 83.3% when the correct adjustment for platelets and cryoprecipitate units was made (Table 10.15). The corresponding figures for the number of patients who had a donor exposure of

80 or more blood component units in the year were 0.4% and 1.7%: that is, by not accounting for the adjustment required for platelet and cryoprecipitate units, there was a four-fold underestimation of the proportion of patients with a donor exposure of 80 or more blood in the year (Table 10.15).

The adjustment required to account for the use of platelet and cryoprecipitate units was also considered in the context of published figures for the risk of transfusion-transmitted infection. The published figures are for the risk per donated unit rather than per used unit: therefore, because platelet and cryoprecipitate units are created from pooled donations, the risk per platelet unit and cryoprecipitate unit used is underestimated unless the relevant adjustment is made (Table 10.16).

Table 10.16 Risk of transfusion-transmissible infections: risk per donated blood component unit and actual risk to patient

		Risk of transmission in blood component per:		
Infection	**Published figure***	**1 *donated* BC unit**	**1 *used* RBC unit**	**1 *used* PLT unit**
Hepatitis B	around 1 in 100,000	0.00001	0.00001	0.00005
Hepatitis C	less than 1 in 400,000	0.0000025	0.0000025	0.0000125
Bacterial	around 1 in 500,000	0.000002	0.000002	0.00001
Malaria	around 1 in 1,000,000	0.000001	0.000001	0.000005
HIV	less than 1 in 4,000,000	0.00000025	0.00000025	0.00000125

* McClelland, 2007. HIV: Human immuno-deficiency virus

Whilst full survival analyses have not been attempted for the study data it was calculated that 48% of all patients in the study dataset had died during the four years between the study year and the year of data extraction and linkage with GRO death records (2004). 132 of the 200 patients (66%) who had a donor exposure of 80 or more had died by 2004. More patients would have died in the intervening years between 2004 and the current year, 2007: a new record linkage with GRO death records is required to update this information. The limitations of the study data notwithstanding, the donor exposure of patients with and without a date of death recorded in their SMR01-CD record are reported separately (Table 10.17).

Table 10.17 Donor exposure for patients with and without GRO death record

Total Donor Exposure for 2000	Patients without death record (% patients alive †) n=6,196	Patients with death record (% patients died †) n=5,798	% Patients to have died by stated date †
1-9	5,407 (87.3)	4,581 (79.0)	45.9% died by 30.03.04
10-19	464 (7.5)	646 (11.1)	58.2% died by 15.03.04
20-29	138 (2.2)	209 (3.6)	60.2% died by 25.02.04
30-39	39 (0.6)	96 (1.7)	71.1% died by 08.04.03
40-49	27 (0.4)	52 (0.9)	65.8% died by 15.03.03
50-59	21 (0.3)	37 (0.6)	63.8% died by 10.01.04
60-69	16 (0.3)	26 (0.4)	61.9% died by 09.12.03
70-79	16 (0.3)	19 (0.3)	54.3% died by 16.08.03
80+	68 (1.1)	132 (2.3)	66.0% died by 11.02.04

Note: All adjusted figures, that is, accounting for corrections for platelet and cryoprecipitate units.
† Correct at time of study data extraction, March 2004

10.6.4. Overview of donor exposure analyses

Donor exposure is a measure of the number of donors to whom blood recipients are exposed via transfusion over a specified period of time. It is calculated as the number of units used for adult dose red blood cell and fresh frozen plasma but for platelets and cryoprecipitate an additional multiplication factor must be taken into account because a unit of each is pooled from five and six donor sources respectively.

Donor exposure is important to quantifying total, residual infection risks posed to recipients of multiple units of transfused blood components. Particularly, current concerns focus on the risk of infection with vCJD transmitted through blood transfusion, a risk which is apparent but small, and largely unquantifiable as it depends on the prevalence of infection in the population and subsequent patterns of donation and transfusion. The findings reported here show how the risk of infection per unit of blood donated underestimates the actual risk per patient. However, the public health impact of high use of blood components by multiply-transfused recipients may be mitigated to an extent by relatively short survival of these patients.

10.7. Overview of alternative applications using study data for analyses of blood component use

The findings reported in this chapter describe a range of applications for which the study dataset could be used to further analyse blood component use. Two practice interventions were described: the use of a best practice indicator for transfusion in total hip replacement (THR) surgery and the use of intra-operative cell salvage in coronary artery bypass graft surgery (CABG). Practice variations were reported in the number of red blood cell units used per procedure performed in both settings (THR practice range, 0.6-2.2 RBC units per procedure performed; average 1.3 RBC units; CABG practice range, 1.4-3.8 RBC units per procedure performed; average 2.9 RBC units). Furthermore, the findings of the modelling analyses reported potential reductions in red blood cell use when the interventions were applied to transfusion practice. Particularly, the modelling analyses for coronary artery bypass graft surgery demonstrated that by utilising a best practice target, savings could be achieved (24.4% RBC units saved) that were comparable to the potential savings that could be achieved using intra-operative cell salvage (range 15.6%-36.6% RBC units saved). Further, the analysis of the condition Thrombotic thrombocytopenic purpura demonstrated how blood component use for a group of patients with a specific condition could be identified and revealed that there are potentially large savings in fresh frozen plasma use (73.0% total FFP units) to be made if transfusion guidelines were to be reconsidered in the light of new evidence for effective and appropriate use of plasma. Together, these findings demonstrate the importance of ongoing efforts to reduce the use of blood by revising and implementing transfusion protocols that should be based on appropriate, comparable evidence of the effectiveness of interventions in reducing the need for allogeneic transfusion whilst avoiding detriment to the patient.

Perhaps the largest influencing factor on future blood use is the ageing population. Modelling analyses were used to describe the contrasting use of blood by the young and elderly; for the Scottish population's total red blood cell use, it was demonstrated that a marked increase in red blood cell use in future years (1.2% increase in RBC units per year) is predicted in comparison with, relatively, very small fluctuations in the size of the population. Specifically, the trend of increasing use of blood in future years was described for total hip replacement procedures, a common surgery in the elderly. Furthermore, the impact of an

ageing population on the blood supply is likely to be aggravated by the predicted reduction in the size of the younger population that represents potential blood donors.

Finally in this chapter, patients' total donor exposure for one year was described for all transfusion recipients in the study. Donor exposure is a topic of particular pertinence given current concerns regarding the transmission of vCJD through blood transfusion. The study dataset was used to identify patients with a high total donor exposure as a result of the transfusion of multiple units of blood or, specifically, the high use of platelet and cryoprecipitate units. The number of patients with a donor exposure of 80 or more is four times greater than initially expected, after the adjustment to donor exposure calculations is made to account for the use of platelet and cryoprecipitate units. In addition, it was demonstrated that it is important to use and report the correct data for total blood use, specifically in relation to the residual transfusion-transmitted infection risks posed by a single unit of used blood, compared to risk values published for units of donated blood. Thus, the findings emphasise the need for safe and effective transfusion that is given only where clinical benefit outweighs the risks of transfusion.

11. DISCUSSION

11.1. OVERVIEW OF DISCUSSION

The study reports on the population of transfusion recipients at hospitals served by SNBTS blood banks using the MAK-Progesa (SNBTS/Progesa) computer system in Eastern regions of Scotland for one year, 2000, for which clinical data in the form of SMR01-CD records was available. The characteristics of transfused and non-transfused populations, the use of individual blood components, and blood use attributed to surgical and haematological case groups have been described. Alternative applications of the study data were explored and modelling analyses to estimate the impact of changes in factors affecting transfusion practice were undertaken.

The following discussion describes the results for blood component use and specifically for red blood cell use that was attributed to surgical and haematological case groups in the context of previous published evidence; discusses the additional applications for which the data was used to explore the effect of methods to reduce allogeneic transfusion; addresses the strengths and weaknesses of available data and the methodology developed and employed in this study; and describes areas of future work in which alternative or additional approaches are considered.

11.2. DISCUSSION OF RESULTS OF STUDY

In this section the key findings reported for this study are discussed in the context of the findings of previously published evidence. The study dataset was described in Chapter 6, the findings illustrating that it was possible to link two independent, routine datasets to create a single dataset that could be used to analyse blood component use. Chapter 6 also presents the findings of analyses of clinical coding variables that were carried out to gain an understanding of the available clinical data and further, to validate the inclusion of major red blood cell using procedures and haematological conditions that were defined for the study. The red cell using procedures were most often coded in the primary OPCS-4 variable, and the haematological malignancies were often coded in the primary ICD-10 variable. The findings support the ISD coding convention for the order of priority by which clinical data should be coded in clinical variables in SMR01 records, thereby supporting the decision to select those particular red cell using procedures to describe important clinical events. The rules devised to resolve issues of competition are discussed separately in section 11.3.4, where it is concluded that the methods employed in this study were appropriate.

Further, the study dataset was used to describe the population of patients who were transfused with red blood cells, platelets, fresh frozen plasma and cryoprecipitate thereby providing blood use data for the study population and demonstrating that the study dataset and methods could be successfully employed for this sort of analysis (Chapter 7) (section 11.2.1). Objectives of this study also included exploring blood component use by clinical case group, and specifically, red blood cell use by surgical case group and haematological case group were described (Chapters 8 and 9) (section 11.2.2 & 11.2.3). Finally, other potential areas of applications for the study dataset in blood component analysis were explored (Chapter 10) (section 11.2.4). The results of analyses that address each objective are discussed here with reference to previously published reports and to the clinical importance of the findings

11.2.1. Describing the transfusion of red blood cells, platelets, fresh frozen plasma or cryoprecipitate units

The findings reported in Chapter 7 provide comprehensive data on the use of blood by age, gender and intensity of transfusion for each blood component type. The data described relates to transfusion day records of units used that were included in the dataset and therefore underestimates the use of blood components by not including those transfusion recipients for whom no SMR01-CD could be linked (Table 6.10). The findings are discussed here in the context of previously published evidence, with a particular focus on red blood cell use. Red blood cell transfusion is the most common blood component transfusion; specific studies of other blood components are available too but from a resource planning perspective red blood cell transfusion has the largest impact on donor, clinical and transfusion services.

The transfusion data that can be used to describe transfusion recipients, transfusion day records and blood component use are reported in two ways: red blood cell, platelet, FFP and cryoprecipitate use are reported separately for each approach. Using red blood cell use as an example, the findings are reported for any transfusion day record of red blood cell units used regardless of the use of other blood components recorded in the same transfusion day record (Table 7.1) and for patients transfused only with red blood cell units when component use was aggregated by patient (Table 7.2). The findings indicate that during the study year most patients (86.5%) transfused with red blood cell units only receive red blood cell units. Conversely, patients transfused with the other blood component types are usually transfused with a combination of blood components, and this is particularly true for cryoprecipitate which is almost never transfused alone: 15.8%, 12.2% and 1.2% of patients transfused with platelets, FFP and cryoprecipitate, respectively, are transfused with those components alone. Blood component use and single blood component use, such as was described here, are not reported for any comprehensive, descriptive studies of clinical blood use reviewed in the this study (section 3.5).

In this study the 47.1% of red blood cell recipients who were male received 52.0% of the total red blood cell units used in the study: total red blood cell use by males and females is roughly equal in this study (Table 11.1). For some studies it is reported that females are

more often transfused, or transfusion recipients are more often female, but the actual number of units transfused by gender shows that males are transfused at a higher rate and therefore the overall proportions of units transfused by gender are roughly equal, as in this present study (Cook & Epps 1991; Mathoulin-Pelissier *et al*, 2000; Palo *et al*, 2006a & 2006b; Vamvakas & Taswell, 1994). The variation between studies might be due to differences in the study setting and population as well as a temporal effect given the broad range of years for which data is reported. Unlike the present study, few studies report both the percentage of patients and percentage of units transfused by age and gender.

Table 11.1 Comparison of transfusion recipient demographics

Study	Males		Aged > 65 years	
	% RBC recipients	% RBC units used	% RBC recipients	% RBC units used
Cook, 1991	49	.	49	.
Vamvakas, 1994	45	48	54	53
Zimmerman, 1997	.	60	.	37
Mathoulin-Pelissier, 2000	50	.	57	.
Wells, 2002	.	51	.	57
PhD STUDY, 2007 (data for 2000)	48	52	59	56

Note1: Study reference is first author and year of publication. Note2: Reports reviewed in section 3.5 only.

Blood component use by age, and especially by the older age groups, has been commonly reported in previous studies. In the present study patients who were aged 65 years or over constituted 58.6% of red blood cell recipients and used 56.1% of red blood cell units used in the study. Thus, the findings of this study indicate that a high proportion of red blood cell use is by older age groups. Earlier studies report slightly lower proportions of patients and red blood cell units used by recipients aged 65 and over which likely reflects the changing demographics over time but relevant denominator data is not reported in the studies to be able to determine this with accuracy (Table 11.1). In general the findings of this study are similar to published reports; furthermore, there may be population differences that make the elderly in some populations have a higher demand for blood, thereby accounting for

variation between studies. For example, Scotland's high rates of heart disease (which requires high blood using CABG surgery) and alcohol abuse (which implicates increased liver transplantation, also a high blood using surgery) mean that the affected age groups would have a high demand for blood, further to the growth in the size of the elderly population.

The importance of quantifying the use of blood by patients aged over 65 years in response to a growing, ageing population was reported for the USA many years ago (Friedman, Burns & Schork, 1979). Older patients are recognised as a group with the potential to use a high proportion of blood because anaemia is less likely to be tolerated well and because of the likelihood of complications of primary disorders. Thus, for an ageing population, such as that of the UK, the impact of demographic change on clinical and transfusion practices is important. Specific calculations of the five year age group data reported by Wells *et al* (2002) gives a value of 65.8% of red blood cell use is transfused to patients aged 60 years or over, which is in good agreement with the findings of the present study. Further, interest in the effect of recipient age on blood component use has been demonstrated in a recently published report claiming to be the first population-based study of blood use by patients aged 65 years and over (Anderson *et al*, 2007). The report described increasing use of red blood cell units per patient up to the age of 85 after which the average red blood use per patient declined, which may be due to the patients being too frail to tolerate surgery or high volume transfusions. Further, the study reported a strong correlation between surgical procedures and blood use. This finding contrasts with other reports that describe increasing blood use for medical conditions in relation to advancing age (Wells *et al*, 2002; Wallis, Wells & Chapman, 2006). The age-related distribution of blood use for surgical and medical case groups was not investigated in this study: however, it was noted that the average age for red blood cell recipients who could be linked with one red cell using procedure was slightly higher (67.0 years, SD 16.2) than those recipients who had two red cell using procedures (50.6 years, SD 22.3), and red blood cell recipients who underwent one or more procedure were similar in age (66.6 years, SD 16.6) to those who had any haematological medical condition during the study year (64.2 years, SD 21.4) (Tables 8.1 & 9.1).

The use of blood components by age was explored further by modelling the effect of the ageing demographic profile of Scotland on the future use of red blood cell units (findings

described in section 10.6). In summary, the estimates suggest that between 2000 and 2016 a 1.2% rise in the growth of the population corresponds to an overall increase in red blood cell use of 18.8%, and between 2016 and 2031 a decrease in the size of the population of 1.2% corresponds to a further 17.9% increase in red blood cell use. The detailed findings describe a decline in the population of younger age groups (under 40 years in 2006 and under 60 years in 2031), the very age group providing the potential blood donor population, as well as an expansion in the older age groups for whom a high rate of transfusion has been described. Therefore, by projection of the population alone a double-edged effect of reduced blood supply and increased demand for blood can be anticipated for the future. Ongoing investment in strategies for donor services and the effective use of blood is likely to be required.

It is acknowledged that the projections modelled for this analysis were based simply on the age and gender specific rates of red blood cell transfusion reported in this study and do not take into consideration changes in clinical and transfusion practice or changes in the epidemiology of disease in the population. Wells *et al* (2002) also applied population projections to age specific rate of transfusion to estimate the change in the future demand for red blood cells, citing the issue of the ageing UK population as a driving force for the analysis; no specific alterations were reported to have been made to account for changes in other factors that may affect the future use of blood. The time frame examined was shorter than that examined for the present study: red blood cell use was estimated to increase by 2.0% between 2000 and 2003 and increase by 4.9% between 2000 and 2008, which equates to red blood cell use increases of 0.7% and 0.6% per year compared to the greater increase of 1.2% per year estimated for the longer projection in the present study (Wells *et al*, 2002). The difference in results could be due to differences in the patient case mix or transfusion practice of the two study settings, or due to the variation in population projections employed.

In addition to age and gender distributions, the intensity of blood component use was described for recipients. The intensity of transfusion was defined in this study as the number of units of individual blood component used in the study year by a patient. Transfusion day records were aggregated by patient identifier and all transfusion day records in the study dataset were included. Therefore, all transfusion events are included, regardless of whether patients have, for example, a single transfused surgical episode or

whether the event was followed by unrelated transfusion events during the year for other surgical procedures or medical conditions.

Overall, for red blood cells, platelets and fresh frozen plasma, but not cryoprecipitate, the distribution of recipients by intensity of transfusion demonstrates a positive skew such that a small proportion of patients (6.8%-11.3% of blood component recipients) are transfused intensively and account for a substantial proportion of blood component units used (42.3%-56.3% of blood component recipients). Furthermore, the most common intensity of red blood cell use per transfusion day record and per patient is two units of red blood cells: the findings relate to the ongoing debate regarding the commonly observed transfusion practice of two-unit transfusions. There are mounting efforts to encourage unit-by-unit transfusions with checks of haemoglobin levels after each unit, thereby conserving the blood supply and reducing recipients' exposure to allogeneic blood (Palo *et al*, 2006a; Titlestad *et al*, 2001; Mallett *et al*, 2000; Ma *et al*, 2005; Grey *et al*, 2006; Boralessa *et al*, 2000). The modal intensity for platelet and cryoprecipitate use reported by this study is one unit per transfusion day record and one unit per patient; for FFP the modal intensity is one unit per transfusion day record and three units per patient. The approach to analysing the intensity of transfusion adopted in this study is one way to address the issue of the time continuum encountered when examining continuous data such as this. The approach adopted by other studies will depend on the question being asked of the data, for example Titlestad *et al* (2001) approaches this issue by reporting on blood component units used per patient per hospital admission. Therefore, by considering various approaches, the intensity of transfusion could be described per transfusion event, admission episode, continuous inpatient stay, or other time period such as one year depending on the measure that is of interest.

In conclusion, the characteristics of the populations transfused with blood components reported by this study provide evidence for the distributions of blood component use by age, sex and intensity of transfusion that are comparable with previous published reports. In particular, the findings support the awareness of older transfusion recipients as large users of blood and demonstrate that the data can be used to estimate the marked effect of an ageing population on the use of blood in Scotland for future years.

11.2.2. Describing the use of blood components by clinical case group: surgery

The lack of a common set of conventions for reporting blood use by clinical reason for transfusion has been identified as a key objective for studies of this sort (section 3.5 & 3.6). For example, it means rather little to simply classifying transfusion events as "surgical", or other broad, surgical case groups that contain multiple procedures and are classified by incomparable groups such as surgical specialty or clinical directorate. Rather, clinical groups based on internationally recognised clinical coding systems such as ICD-10 should enable comparable classification and reporting of results across different studies.

The blood attribution rules devised for this study were employed to attribute blood use to specific clinical case groups that represent the likely underlying reasons that can explain why a patient was transfused. This study defined specific, individual red cell using procedures or small clusters of very closely related procedures using the OPCS-4 coding system. The procedures included were based on clinical knowledge of clinical and transfusion practices, and on the surgical procedures commonly cited in maximum surgical blood ordering schedules (MSBOS). Because those guidelines identify procedures that are significant users of blood, being either commonly or heavily transfused, and that are considered to be appropriate targets for reducing surgical red blood cell use, MSBOSs were a useful reference for guiding the definition of notable red cell using procedures.

The red cell using procedures could otherwise have been defined experimentally using data-driven approaches. However, instead of pursuing the data-driven approaches in the early stages of this study it was decided to use the list of procedures as an initial attempt so that progress could be made in the definition and validation of subsequent methods. Some initial investigations into a data-driven approach have already been considered for future work as it is acknowledged that changes could be made to potentially improve the accuracy and relevance of the procedures studied, thereby affecting the overall reporting of blood use by surgical case group (Section 11.4). The findings of this study are reported with this understanding of potential limitations and with the acknowledgment that the number of red blood cell units attributed to surgical case groups might be greater if additional, relevant red cell using procedures were included.

By using these specific blood attribution rules an inference is made about the reason for transfusion. It is acknowledged that this inference cannot represent the only or absolute reason for transfusion and different blood attribution rules would provide a different view of the data. Indeed, in this study, where a transfusion day record can be attributed to both a surgical procedure and a haematological diagnosis the overlap in blood use can be quantified (Figure 9.3), demonstrating an acceptance of the potential for alternative plausible explanations for defining transfusion events. Further, it is acknowledged that the methods employed in this study were based on assumptions relevant to the current context of clinical and transfusion practice, and as such, the results should be interpreted in this context alone. The findings for blood use attributed to specific procedural case groups for this study are discussed here in the context of the assumptions made for this study and in relation to previous evidence for blood use by surgical case group.

Overall, 28.9% of the red blood cell units used in the present study could be attributed to the specified surgical case groups, a lower proportion of total red blood cell use than is reported for previous studies in which blood use was linked with "surgical" or "medical" classifications. The proportion of red blood cell units attributed to "surgery" in previous studies (reviewed in section 3.5) ranges from 70% in the earliest report to 33% in the most recent report (Table 11.2). The variation is explained in part by the way in which the definition of surgery varies depending on the source of clinical data (for example, by department, from discharge letter, from blood request form, by survey) and by the clinical classification systems used. If the definitions are considered to be comparable then the findings are illustrative of a trend of decreasing blood use in surgery, and elective surgery in particular, which echoes a general trend that is indicative of improvements in surgical and anaesthetic techniques, the introduction of alterative blood conservation interventions, such as intra-operative cell salvage, and changes in the education, attitudes and awareness of clinicians (Wallis, Wells & Chapman, 2006; Karkouti *et al*, 2001; Lemos & Healy, 1996). Further, the findings are perhaps evidence that these reports have acknowledged and addressed the requirement to examine medical or diagnostic reasons for transfusion when describing blood use by clinical case group.

Table 11.2 Red blood cell units attributed to surgical and medical case groups

Study	RBC units used attributed to Surgical : Medical	Notes on methodology and case groups
Cook, 1991	70:30	100% of attributed RBC units reported
Vamvakas, 1994	55:45	100% of attributed patients reported (NB. not units used)
Zimmerman, 1997	50:30	Remaining 20% of RBC units attributed to "other specialties"
Mathoulin-Pelissier, 2000	47:53	100% of attributed patients reported (NB. not units used)
Titlestad, 2001	57:43	100% of attributed RBC units reported
Wells, 2002	41:52	Remaining 6%of RBC units attributed to Obstetrics & Gynaecology and 1% not attributed
Stanworth, 2002	51:36	Remaining 13% or RBC units attributed to "combined" specialties
Wallis, 2006	33:62	Remaining 5% attributed to Obstetrics & Gynaecology
PhD study, 2007 (data for 2000)	23:67	Medical use is all units not attributed to surgical case groups (including 12% to haematological conditions)

Note1: Cross-reference Table 3.4a: figures rounded up in Table 11.3 compared to Table 3.4a. Note2. Studies referenced by first author and year of publication: data reported for previous study period. Note3. Reports reviewed in section 3.5 only; additional reports compared to Table 3.4a to include reports for which this information could be ascertained or deduced rather than specific studies of blood use by surgical/medical classification.

Of the surgical case groups specified for this study the three that account for the largest proportions of red blood cell use attributed to procedures are: primary coronary artery bypass graft operations (21.2% of RBC units attributed to surgical case groups), primary total hip replacements (10.3% of RBC units attributed to surgical case groups) and operations on valves of the heart and adjacent structures (8.1% of RBC units attributed to surgical case groups). The top three ranking procedures in terms of red blood cell units used per operation performed are transplantation of liver (10.2 units), emergency replacement of aneurysmal segment of aorta (8.1 units), and other operations on aorta (4.6 units). By surgical specialty, the three highest users of red blood cell units for this study are cardiovascular (41%), orthopaedic (34%) and gastrointestinal (13%) (Table 11.3).

Table 11.3 Summary of reported top surgical case groups for red blood cell use

Study	Surgical case groups (% of total RBC units used attributed to procedures)
Chiavetta, 1996	Digestive system (23) Cardiovascular (18) Muscoskeletal (17)
Titlestad, 2001	Cardiovascular/thoracic (50) Urology (21) Obstetrics & gynaecology (6)
Wells, 2002	Orthopaedics (14) General surgery (10) Cardiothoracic surgery (6)
Stanworth, 2002	General surgery & orthopaedics (50) Cardiothoracics (16) Obstetrics & gynaecology (10)
Wallis, 2006	Orthopaedics (19) Gastrointestinal & liver (16) Cardiothoracics (16)
PhD study, 2007 (data for 2000)	Cardiovascular (41) Orthopaedics (34) Digestive system (13)

Note1: Cross-reference Table 3.4c: figures rounded up in Table 11.3 compared to Table 3.4c; Table 3.4c classifications generalised whereas Table 11.3 classifications as described in original reports. Note2. Studies referenced by first author and year of publication. Note3. Reports reviewed in section 3.5 only.

There is a large body of published evidence for blood use for a range of elective surgical procedures, including recent large-scale studies that report for a wide range of surgical procedures (section 3.3 and 3.4), and particularly for coronary artery bypass graft operations and joint arthroplasty with respect to the proportions of patients transfused and the proportions of units transfused per patient, the determinants of transfusion, patient characteristics, and variation between hospitals and across procedure types (Surgenor *et al*, 1992; Surgenor *et al*, 1996; Goodnough, Johnston & Toy, 1991; Goodnough *et al*, 1989; Chiavetta *et al*, 1996; Stanworth *et al*, 2002; Cobain *et al*, 2007; Hasley *et al*, 1995; Hutton *et al*, 2005; Sirchia *et al*, 1994; Wells *et al*, 2002). However, few published reports provide blood use data for a range of individual, well-defined procedures: surgical blood use data is commonly reported in other studies by surgical specialty or similar sub-category of surgical classification. Surgical case groups of this type that account for a high use of red blood cell

units are gastrointestinal, cardiothoracic/cardiovascular, and orthopaedic procedures (Table 11.3). In this respect the results of this study are comparable to published evidence, although this could be anticipated since the inclusion of red cell using procedures was influenced by knowledge of such previous results and similar clinical experiences of red blood cell use. The variation between these studies in the classifications reported for cardiovascular and cardiothoracic procedures specifically is noted. Further, the findings compared in Table 11.3 are the percentages of red blood cells attributed to surgical case groups. These cannot distinguish procedures that are frequently performed but have a modest use of blood compared with procedures that have low incidence but are associated individually with a high use of blood.

For joint arthroplasty specifically, the evidence suggests that there is wide variation within and between hospitals for the measures of rates of transfusion as well as across procedure types and patient groups (Wells *et al*, 2002; Maxwell *et al*, 2002; Hasley *et al*, 1995; Sirchia, 1994; Spencer *et al*, 2005; Lemos & Healy, 1996; Surgenor *et al*, 1991; Bierbaum *et al*, 1999; Hutton *et al*, 2005; Boralessa *et al*, 2000 & 2001; Churchill *et al*, 1998). Although describing inter-hospital variation was not a specific aim of this present study, overall the findings agree that orthopaedic surgery and specifically total hip and knee replacement procedures account for a large proportion of total red blood cell use for the study population, suggesting that orthopaedic surgery might be an area worth targeting with developments in blood conservation strategies. Strategies include, for example, reducing blood loss in joint replacement surgery by the use of cement fixings and by specific surgical practices relating to the timing of removal of tourniquets and the use of wound compression dressings (Lemos & Healy, 1996); intra-operative cell salvage (section 11.4); and the increased use of endoscopic, "key-hole", surgery reduces the requirement for blood (Lemos & Healy, 1996; Huët *et al*, 1999; Carless *et al*, 2006).

Thus, the findings of the present study describe areas of high blood use, for both the total number of units used and units used per operation performed. This application of the data is supported by evidence for the role of national arthroplasty registers, such as in Sweden and the UK, in identifying poor outcomes that are associated with surgery as well as for benchmarking practice for the future (Burns & Bourne, 2006; Scottish Arthroplasty Project, 2007). For example, in Sweden the national arthroplasty project has demonstrated

reductions in the number of different types of implant used as well as reductions in the number of revision operations being performed (Burns & Bourne, 2006). With the overall number of total hip and knee replacements, and subsequent revisions that are particularly associated with increased costs and poorer outcomes, on the increase and with the trend expected to worsen in the future due to the ageing population, at least in the UK, targeted clinical and transfusion practice improvements in the area of joint replacement surgery are recommended (Burns & Bourne, 2006; Scottish Arthroplasty Project, 2007). Thus, accurate and timely evidence for trends in blood use, such as can be provided by the present study, the epidemiology of related diseases, and population demographics should be monitored and the information used to aid decisions about requirements for practice change in the way blood is used or to inform resource planning.

Previous reports also cite obstetrics and gynaecology as a well-defined clinical case group to which a reasonable amount of blood can be attributed. The SMR01 clinical data extracted for the present study could not be linked with specific maternal or neonatal (SMR02 and SMR11) hospital records and so obstetric and gynaecological blood use was not fully described for this study. By examining the blood use for obstetric and gynaecology case groups for other studies, it was noted that, as for other areas of surgery, the precise case group classifications vary between studies: obstetrics and gynaecology has been classified as a specific surgical specialty (6% and 10% of RBC units attributed to surgical case groups , Titlestad *et al*, 2001 and Stanworth *et al*, 2002, respectively), a specific medical specialty (1% and 7% of RBC units attributed to medical case groups, Mathoulin-Pelissier, 2000 and Lim *et al*, 2004, respectively), and also as a separate group that bridges surgical and medical specialties (4%, 5% and 6% of all RBC units used per study, Zimmerman *et al*, 1997, Wallis, Wells & Chapman, 2006, and Wells *et al*, 2002, respectively). Obstetric and gynaecological diseases and procedures, classified by the CPHA[6] List A Hospital Diagnosis Groups, were reported to account for 4.9% of all blood component units used and 6.7% of transfusion recipients by Friedman, Burns and Schork (1979). Therefore, the findings of previous studies suggest that between 1% and 10% of used red blood cell units could be potentially attributed to obstetrics and gynaecology if the appropriate record linkage was carried out to link SMR02 and SMR11 data schemes with the study dataset. Furthermore, the reports suggest that relevant,

[6] CPHA: Commission on Professional and Hospital Activities (America)

comparable case group definitions and approaches to describing blood use in the area of obstetrics and gynaecology, and others, are needed for the future.

11.2.3. Describing the use of blood components by clinical case group: haematology

The haematological case groups reported for this study were the pre-malignant conditions myelodysplastic syndromes or polycythaemia vera and the malignant conditions lymphoma, myeloma and leukaemia, that were defined using ICD-10 codes. Overall, 12.1% of red blood cell use in the study could be attributed to these haematological conditions. Previous studies that included diagnostic analysis of red blood cell use report the percentage of red blood cell units attributed to haematological case groups as 10.0% diseases of blood and blood-forming organs combined with leukaemia, lymphoma and myeloma, 14.0% to leukaemia and lymphoma combined with diseases of blood and blood-forming organs, 42.0% and 28.2% to all neoplasms, and 15.5%, 36.3% and 30.0% to "haematology" (Chiavetta *et al*, 1996, Zimmerman *et al*, 1997; Mathoulin-Pelissier *et al*, 2000 and Lim *et al*, 2004; Wells *et al*, 2002, Stanworth *et al*, 2002, and Wallis, Well & Chapman, 2006, respectively) (Table 11.4). The findings, and to an extent the classifications, for Chiavetta *et al* (1996), Zimmerman *et al* (1997) and Wells *et al* (2002) are in good agreement with the findings of the present study. Mathoulin-Pelissier *et al* (2000) and Lim *et al* (2004) report all neoplasms together: the case group includes the ICD-10 codes included in the present study but also many additional conditions and so the proportion of red blood cell units reported for the case group is not high in comparison with the results reported for other studies (Table 11.4).

In general, the range of findings for blood use attributed to haematology reflects the differences in the classification of case groups. Findings can only be compared where a full description is available for how the case group was defined: for example definitions may be by specific "haematology" category (either defined by medical specialty or by the researchers), or may cover various clinical codes for specific haematological neoplasms and/or diseases of the blood and blood-forming organs. In general, even where well-defined, the classifications for haematological conditions are comparatively broad. A strength of the

present study is that the haematological case groups are defined by specific, individual or small groups of ICD-10 codes.

Table 11.4 Comparison of results for haematological blood use

Study	% RBC units attributed to medical case groups	Notes on haematological case groups
Chiavetta, 1996	10.0	BDC IV, 280-289 + BDC 203-205
Zimmerman, 1997	14.0	BDC I, 200-208 + BDC IV, 280-289
Mathoulin-Pelissier, 2000	42.0	ICD-10 codes C00-D48
Wells, 2002	15.5	"Haematology" (survey form case group)
Stanworth, 2002	36.3 *	"Haematology" specialty or directorate
Lim, 2004	1.0	ICD-10 codes C00-D48
Wallis, 2006	30.0	"Haematology" (survey form case group)
PhD study, 2007 (data for 2000)	12.1	ICD-10 codes C81-85, C90, C91-95, D45&46

BDC: Broad diagnostic category * 44.2% if include all haematology, haematology & general medicine, and haematology & oncology. Note1: Cross-reference Table 3.4b: figures vary by classification reported in tables; Table 3.4b generalised whereas Table 11.4 classifications are as described in original reports. Note2: Studies referenced by first author and year of publication. Note3: Reports reviewed in section 3.5 only

The present study investigated the extent to which attribution of blood component units to individual haematological case groups (though not to "haematological conditions" in total) was influenced by the resolution of intra- and inter-episode competition between haematological conditions at the patient level. The findings demonstrated that there were very few instances where more than one haematological condition could be attributed to a patient during the study period and where it did occur then the conditions were clinically related. These findings suggest that the haematological conditions in the study were appropriately chosen and were representative of a well-defined group of transfusion recipients, and that the haematological blood attribution rule was acceptable for identifying relevant patients. In particular, the combinations of pre-malignant and malignant haematological conditions identified in the study are interesting because they describe typical clinical disease progression and related comorbidities that might be expected for haematological patients. In the study, a large proportion of red blood cell units used were attributed to the case group of pre-malignant conditions (myelodysplastic syndromes or

polycythaemia vera). This is consistent with pre-malignant conditions being the diagnosis that is likely to be made prior to a diagnosis of a malignant condition and in the present study blood is attributed to the patient's first blood using haematological diagnosis. This understanding of clinical disease progression and comorbidities was integral to defining appropriate methods of attribution of blood to haematological case groups; similar understanding will be required for the future development of additional diagnostic case groups, such as for other chronic conditions where the broader clinical history of the patient is also potentially relevant. This discussion, however, raises again the persistent question concerning the actual reason for transfusion, that is, where one condition leads to another or one condition necessitates surgery, what ultimately constitutes the underlying cause of transfusion? This study largely addresses this issue using the practical approach of describing blood use from the likely perspective of the clinicians and hospital transfusion committees who will ultimately make use of reports on blood component use by clinical case group.

Awareness of the use of blood for medical indications has grown as reductions in blood use in surgical contexts are made due to improved surgical and anaesthetic techniques, the use of intra-operative cell salvage and implementation of maximum surgical blood order schedules, for example. Therefore, there is a need to monitor and optimise the use of blood according to well-defined diagnostic case groups. A population based survey of red blood cell use in 2000, in which the use of blood was divided between surgical and medical indications at a ratio of 41:52, prompted a more detailed analysis of the use of red blood cells for medical indications (Wells *et al*, 2002). The second survey four years later reported an overall reduction in total red blood cell units used, and specifically, a reduction in surgical use and an increase in use related to medical indications such as haematology, non-haematological malignancies and gastrointestinal haemorrhage (Wallis, Wells & Chapman, 2006). The report also concludes that the average age of transfusion recipients increased between the two studies and that the proportion of units used for medical indications increased with advancing age (Wallis, Wells & Chapman, 2006).

The evidence suggests that not only is the amount of blood used for surgical procedures decreasing but that the need for blood for patients with medical conditions is increasing. This is likely to be in response to changes in incidence and patterns of disease, changes in

treatment, and improved survival or some combination of these factors. Between 1994 and 2003 the incidence of cancer in the UK has remained fairly constant, with an overall 4% decrease in males and a 3% increase in females (Cancer Research UK, online). Reporting and registration changes have been described specifically for lymphomas: the decrease in incidence of Hodgkin's lymphoma and increase in incidence of non-Hodgkin's lymphoma reflects a change in classification for some cancers from Hodgkin's to non-Hodgkin's lymphoma. Further, myelodysplastic syndromes are considered likely to be reported inaccurately due to difficulties in diagnosing the condition and subsequent classification (Aul *et al*, 1997). Although incidence rates overall are generally falling, the incidence of leukaemia, multiple myeloma and non-Hodgkin's lymphoma increases with age; similarly, myelodysplastic syndromes are also associated with advancing age (Cancer Research UK, online; Aul *et al*, 1997). Therefore, improved survival rates and an ageing population may be expected to have a marked effect in terms of increasing the prevalence of cancers and hence on the use of blood transfusion for supporting chemotherapy treatments as well as increased use in cancer-related surgery (the excision of tumours, for example).

To facilitate analysis of haematological malignancies and cancers in general, a role for specialist cancer registers has been suggested as a requirement for the future (Cartwright, Gilman & Gurney, 1999). The clinical data used in the present study was linked to SMR06, the ISD-held cancer register, but only a single indicator variable for patients' status in the cancer register was provided: full linkage with SMR06 could provide specific oncology data including information on the pathology and treatment of specific conditions. The cancer register should be investigated to elucidate a role for this specific information in future blood use analyses. Further, the International Classification of Disease classification system has been criticised for inappropriate groupings of haematological diagnoses, particularly in the way that different types of leukaemia diagnoses have been aggregated as well as for a lack of detailed classification of pre-malignant haematological conditions. Problems such as these, coupled with decisions regarding the appropriate underlying disease or condition that necessitates transfusion are a challenge to the accurate and meaningful attribution of blood to diagnostic case groups (Cartwright, Gilman & Gurney, 1999; Wells, 2002).

Table 11.5 Summary of reported top diagnostic case groups for red blood cell use

Study	Diagnostic case groups (% of total RBC units used attributed to diagnoses)
Friedman, 1979	Malignant neoplasm (19) Non-malignant gastrointestinal disease (18) Fracture/traumatic soft tissue injury (12)
Cook, 1991	Circulatory system (24) Digestive system (17) Neoplasms (16)
Chiavetta, 1996	Neoplasms (27) Digestive system (18) Circulatory system (16)
Zimmerman, 1997	Non-haematological neoplasms (27) Circulatory system (23) Leukaemia & lymphoma, and diseases of blood & blood-forming organs (14)
Mathoulin-Pelissier, 2000	Neoplasms (42) Injury & poisoning (16) Digestive system (14)
Wells, 2002	Haematology (16) Digestive system (11)
Stanworth, 2002	Haematology & general medicine (all groups) (70) Renal medicine (11) Radiology & oncology (8)
Lim, 2004	Neoplasms (28) Injury & Poisoning (20) Digestive system (13)
Wallis, 2006	Haematology (30) Gastrointestinal haemorrhage (22) Non-haematological neoplasms (14)
PhD study, 2007 (data for 2000)	Haematological malignancies (12)

Note1: Cross-reference Table 3.4b: figures vary due to different classification reported in tables; Table 3.4b generalised whereas Table 11.4 classifications are as described in original reports. Note2: Studies referenced by first author and year of publication. Note3: Reports reviewed in section 3.5 only

In addition to the haematological case groups defined for specific analysis of diagnostic blood use in the present study, other diagnostic case groups have been reported for previous studies, including neoplasms (all classifications, 16-42% of RBC units attributed to diagnostic case groups), circulatory conditions (16-24% of RBC units attributed to diagnostic case

groups) and disease of the digestive system (11-18% of RBC units attributed to diagnostic case groups) (Table 11.5). The commonality of reported diagnostic case groups across previous studies, and to an extent the consistency in findings for the attributed red blood cell use within these case groups, provides a comparable body of evidence and suggests areas for which additional diagnostic case groups could be developed for further analysis of the study dataset (section 11.4).

Also, although blood component use for haematological conditions in the present study, and generally for medical use in previous studies, has focused on red blood cell transfusion, there is evidence for the use of other blood component types for medical indications. For example, malignant diseases alone have been reported as accounting for 57% of platelet use, 38% of which was attributed to leukaemia and lymphoma patients (Zimmerman *et al*, 1997). Platelet transfusion is an essential intervention for leukaemia that enables treatment with chemotherapy. Further, malignant, non-haematological neoplasms and diseases of the digestive and circulatory systems have been reported as notable areas of use for fresh frozen plasma (Mathoulin-Pelissier *et al*, 2000; Zimmerman *et al*, 1997). However, where the effectiveness of fresh frozen plasma transfusion has been analysed by randomised control trial the findings suggest that there is little evidence to support current practice guidelines of FFP transfusion (Stanworth *et al*, 2004). Continued monitoring of blood component use, patient outcome and appropriate trials of blood component therapy and alternative interventions should be encouraged in order to monitor compliance with practice guidelines for the effective use of all blood component types.

Overall, the findings of the present study, in which the proportion of red blood cell units used for haematological conditions was quantified, provide evidence for another area of red blood cell use that is supported by previous studies. As has been described previously, the rule for the attribution of red blood cell units to haematological case groups could be applied to other diagnostic case groups where patients' total transfusion data for a specified time period is relevant to the condition. Taken together, evidence for the increasing use of blood for medical or diagnostic conditions in contrast to decreasing blood use for surgical events, the suggestions for improvements to reporting and classification of medical conditions, and the reports of blood use for other medical or diagnostic conditions and blood component types, suggest that blood component use attributed to medical or diagnostic case groups is

an important area for future blood use analysis. Further, the findings are again evidence to support the recommendation for common methods for classifying and reporting blood use.

11.2.4. Discussion of results for additional applications using study dataset

The final set of analyses carried out for this study addressed the objectives of identifying additional, potential applications which became possible given the creation of the study dataset. Topics of particular clinical interest that were explored include modelling analyses to assess the impact of changes in transfusion practice, for example, the use of alternative interventions, and the impact on the supply of blood and demand for blood due to changes in future population demographics.

Concept of a best practice indicator and practice intervention for reducing allogeneic transfusion requirements

A useful application of the study data was the investigation of the novel concept of a best practice indicator for transfusion. A best practice transfusion indicator is a level of blood use that is representative of low blood use for a specific procedure that is determined by observing the transfusion practice of several surgical teams or across clinical institutions. It should be the lowest observed value, a value in the lowest quartile of the observed performance range, or a similar measure that is clinically effective and achievable. Furthermore, the value of the best practice indicator depends on the assumption that the use of lower rates of transfusion is not associated with any detriment to the patient and so an appropriate measure of outcome is needed in order to assess detriment versus benefit. The value of the best practice indicator will also have to be continually reassessed. In the event that the best practice indicator is not the lowest value of observed practice, but another low value that is not associated with detriment to patient outcome, the aim of reducing the practice of high users may be in part countered by an increase in the practice of low users where it is of clinical benefit to do so. The reality of achieving best practice targets for transfusion is influenced by factors affecting individual institutions and should be supported by the aims and actions of hospital transfusion committees. To estimate the potential impact

of a change in transfusion practice to the use of a best practice indicator, best practice values that were determined at a hospital level by observing practice variation, were modelled here for total hip replacements and coronary artery bypass graft operations.

The range of red blood cell use reported for the study dataset for the number of units used per procedure performed or per patient undergoing a procedure, by hospital, have been described (section 10.3 and 10.4). Applying the lowest reported values for red blood cell use for total hip replacements (0.6 red blood cell units per procedure performed) to the number of procedures in the whole of Scotland in 2000 resulted in a saving of 3,589 red blood cell units (53.8% of total red blood cell units used for total hip replacement procedures in whole of Scotland in 2000) compared to normal practice as observed in the study dataset (Table 10.3). This indicates the potential for savings in red blood cell use for a surgical procedure for which it has been predicted that red blood cell use will continue to increase in the future if no blood conservation strategy or alternative intervention is employed. The introduction of a best practice indicator, with appropriate education and support from hospital transfusion committees, could be an effective way to encourage surgical teams to reduce allogeneic transfusion.

The reported scale of savings in red blood cell use that could be achieved from another blood conservation strategy, intra-operative cell salvage, is discussed next. Intra-operative cell salvage (IOCS) is a mechanical process by which blood that is lost during surgery is recycled and, after washing to remove plasma proteins, is returned to the patient. This intervention can replace or reduce the need for allogeneic transfusion, and thus has the potential to make marked savings in resources of allogeneic blood. Values for predicted red blood cell savings were obtained from published evidence for IOCS in cardiac surgery and were applied to data for coronary artery bypass graft (CABG) operations in this present study to model the potential impact on blood use. CABG surgery was chosen because procedures have a high requirement for blood and the use of IOCS has already been demonstrated in this type of surgery (section 10.4) (Bell *et al*, 1992; McGill *et al*, 2002; Carless *et al*, 2006). The findings of the modelling analysis in this study reported savings in red blood cell use of between 1,300 and 3,046 red blood cell units; 15.6% and 36.6% of the total red blood cell units used for all CABG procedures in Scotland in 2000 in comparison with no intervention (Table 10.7).

Furthermore, the estimated saving in red blood cell use in CABG surgery when a best practice target of 1.4 red blood cell units per procedure performed (Aberdeen Royal Infirmary) was applied was 24.4% of total red blood cell units used for CABG procedures across Scotland in 2000 (Table 10.7). This potential saving falls within the range of savings estimated for the use of IOCS in CABG surgery. Therefore, a change in practice behaviour might be able to achieve savings in the same order as an expensive, technical intervention which poses new risks. It is acknowledged that an intervention such as IOCS might be employed in order to achieve best practice targets, though, where practice has been improved all aspects of patient management and blood prescribing have been better executed. Comparisons such as these are useful to informing practice decisions but these should also be based on analysis of clinical effectiveness, cost effectiveness, the logistics of implementation, resource issues, predicted long-term benefits and sustainability of practice.

The modelling analyses reported in the present study focused on intraoperative cell salvage in coronary artery bypass graft procedures but there is also compelling evidence for its efficacy when used in orthopaedic surgery such as joint arthroplasty. A systematic review of cell salvage in adults undergoing surgery identified 23 studies relating to the use of IOCS in CABG surgery and a further 23 relating to the use of IOCS in orthopaedic surgery: reductions in allogeneic transfusion were reported for both settings, and in fact reductions in allogeneic use were greater in orthopaedic cases than in the CABG settings. It was noted that the quality of all studies reviewed was described as being poor or biased in favour of cell salvage and so appropriately designed studies are recommended for the future (Carless et al, 2006). Post-operative cell salvage, in which blood is collected from patients' wound drains and is either filtered or washed prior to being re-infused, has also been shown to reduce the need for allogeneic transfusion (Lemos & Healy, 1996). Controversy surrounds the practice given concerns over contamination of the recycled blood but there is also evidence that re-infusion of unwashed post-operative cell salvaged blood has immuno-stimulatory effects which may be advantageous in fighting post-operative infection (UK Blood Transfusion Service, online). Indeed, post-operative cell salvage is routinely employed in mainly orthopaedic settings within the UK. This is noteworthy given the modelling analysis in this study that described the effect of the ageing population on increasing demand for blood for primary and revision total hip replacement procedures.

Therefore, given the anticipated changes in demographics, the epidemiology of disease, and changes in clinical and transfusion practice the efficacy of blood conservation interventions should be examined for specific patient populations (for example, the elderly) and for specific clinical case groups, diseases and surgical procedures, in order to identify areas where allogeneic blood use can be reduced. As with all blood conservation strategies, as indeed for allogeneic blood transfusion itself, the balance of risk versus benefit needs careful consideration. The additional costs of IOCS may be considerable but if balanced by the advantages of reduced infection and immuno-modulatory effects and reduced impact on the supply of blood, the intervention could be of considerable benefit in a pressurised and resource-constrained industry. IOCS in CABG and orthopaedic settings is neither related to poorer early outcomes, such as hospital length of stay, post-operative bleeding and mortality, nor to adverse reactions (Carless *et al*, 2006; Davies *et al*, 2006). Evidence for the effective use of other blood conservation interventions in CABG and orthopaedic settings has been reported: pre-operative autologous donation or normovolaemic haemodilution (though not currently encouraged in the UK (DOH, Better Blood Transfusion Toolkit, online)), transfusion protocols and restrictive thresholds, and the use of pharmacological agents (aprotinin, tranexamic acid and erythropoietin for example) (Huët *et al*, 1999; McGill *et al*, 2002; Davies *et al*, 2006; Carless *et al*, 2006). However, there is a need for adequately powered randomised controlled trials and comparative analysis of allogeneic transfusion alternatives to describe the effectiveness and cost benefit of implementation, whilst continuing to monitor the use of blood, such as can be done using this present study's data, in order to identify and assess target areas for intervention with blood conservation strategies (Davies *et al*, 2006).

Clinical effectiveness and best practise: a role for an appropriate evidence base of transfusion efficacy in reducing inappropriate transfusions

The importance of adequate analysis of clinical effectiveness in transfusion practice is exemplified by the analysis of fresh frozen plasma (FFP) use in relation to thrombotic thrombocytopenia purpura (TTP) carried out using the present study dataset (section 10.5). The findings demonstrate how effective monitoring and analysis of specific patient groups in combination with appropriate evidence to inform transfusion practice can be used to

reduce inappropriate transfusion and to conserve the supply of blood components of all types.

The analysis was prompted by a review reporting the lack of evidence to demonstrate clinical effectiveness of FFP transfusion in all conditions for which clinical guidelines describe its use, that is, except in the case of TTP (Stanworth *et al*, 2004; Brunskill *et al*, 2007). The analysis reported for the present study aimed to identify TTP patients and quantify FFP use in comparison with the total number of FFP units used for all clinical indications in the study in order to quantify the potential savings in FFP use in light of emerging evidence about current transfusion practice and effectiveness. TTP patients were not well characterised at the time (2000) and even now the condition is not defined by a specific ICD-10 code. Therefore, patients of interest were defined by the two criteria of being linked to the use of a high number of FFP units and having any diagnosis of purpura or other related haemorrhagic conditions or thrombotic microangiopathy. By these criteria a small number of patients (n=5) were identified who together were the recipients of 2,554 units of FFP, representing 27.0% of the total number of FFP units used in the study (Table 10.13). The conclusions are that the potential exists to make large savings in FFP units (potentially 73.0% according to data in this study) if recent evidence for the clinical effectiveness of FFP transfusion is observed and guidelines reconsidered; and that the study dataset can be used to describe blood use for all blood component types and for specific groups of patients.

Donor exposure and vCJD

Donor exposure is a measure of the number of donors to whom blood recipients are exposed though blood transfusion. The concept of donor exposure was investigated specifically to identify patients who are transfused with many units of blood components and who are therefore at increased risk of transfusion transmitted infections and errors of wrong blood transfusion (section 10.5). The risks of transfusion transmitted infections are typically expressed as the risk per donated unit of blood component rather than risk per unit used and so the risk to the patient is underestimated for the transfusion of units of platelet and cryoprecipitate, which are pooled from multiple donated units. The compound risk of

infection for a patient who receives multiple transfusions is a concept that has not been fully acknowledged by transfusion practitioners.

By describing donor exposure for patients in the present study the effect of the adjustments made for calculating exposure for platelet (units used multiplied by five) and cryoprecipitate (units used multiplied by six) use was elucidated (Tables 10.14 & 10.15). By not accounting for these adjustments the number of patients with a donor exposure of 80 or more was underestimated by a factor of four (4.2% of all patients, unadjusted, versus 16.8% of all patients, adjusted). A donor exposure of 80 or more transfusions per patient throughout a lifetime is the recent estimation of the threshold donor exposure after which a patient is considered to be at particular risk of vCJD infection, though not necessarily disease contraction (Dobra, personal communication). Since this estimate is likely to change with new epidemiological data, donor exposure for all patients was reported for the present study. For public health purposes there are important practical implications for the management of patients who are considered to be at risk of vCJD and so it is important to have estimates of the number of patients in the high risk category, however that might be defined.

Furthermore, the findings reported are for donor exposure in one year and there are expected to be patients who have had transfusions prior to or subsequent to the study period, therefore, the findings of this study are a minimum estimate for patients' total lifetime exposure to blood. Given that the risk to the patient increases with each transfusion to which the patient is exposed it is important to consider the overall transfusion-associated risk for a patient for all blood component units received in a lifetime. Following death, patients are evidently at no further risk of receiving a transfusion, but the latent phase of the disease means that they may have been infected without being symptomatic at the time of death. The findings of the present study report donor exposure for patients with and without a record of date of death (up to 2004) to provide a first insight into donor exposure in relation to survival for which specific future analyses are suggested. It is acknowledged that because the study data contains at the most one year's transfusion data for the study population and because up to date death record data was not sought, the findings are only indicative of the potential to establish an individual's total exposure to blood, in relation to infection risks and survival, where appropriate, that is, comprehensive, national data covering a period of several years is available.

It is well-documented that reductions in the use of blood should be made wherever possible in order to reduce adverse events and reactions associated with transfusion, and this is especially true for those who are heavily transfused (McClelland, 2007; SEHD, 1999a & 1999b; JPAC, 2007). Prior to the emergence of vCJD, there was confidence that blood transfusion was highly safe in terms of transfusion transmissible infection, far safer than ever before. The emergence of vCJD and evidence for the potential risk of vCJD transmission through blood transfusion has become one of the main concerns surrounding transfusion practice and particularly the transfusion of multiple units per patient (SEHD, 1999b; Llewellyn *et al*, 2004). Under new UK regulations introduced to control the spread of vCJD, surviving transfusion recipients are subsequently excluded from donating blood (JPAC, 2007; SEHD, 1999b). Other regulations introduced thus far in the UK relate to the use of, and subsequent cleaning or disposal of, surgical instruments as surgical instruments have been implicated in the transmission of vCJD from infected patients undergoing surgery, regardless of the transfusion risk or donor status of these patients. CJD contracted through accidental transfer during a medical intervention such as via surgical instruments, organ and tissue transplants and indeed blood transfusion is termed iatrogenic CJD. CJD is extremely resistant to chemical and physical decontamination processes meaning that it could not be guaranteed that sterilisation processes would render surgical instruments free of CJD (RCSE, 2001; JPAC, 2007; NICE, 2006).

In 1999 the government recommended the introduction of single-use instruments for high risk procedures involving the central nervous system and eye (particularly tonsillectomy and adenoidectomy but excluding operations involving cerebrospinal fluid except spinal surgery where the outer layer of the meninges is breached) and in 2001 announced a £200 million upgrade of decontamination facilities to improve sterilisation processes for surgical instruments (SEHD, 1999b). However, by the end of 2001 single-use instruments were withdrawn due to concerns that the quality of instruments was reduced and was affecting their safe and effective use in surgery (RCSE, 2001; NICE, 2006). Current precautions recommend comprehensive cleaning and sterilisation procedures on all surgical and diagnostic instruments, the quarantine of instruments used on suspected cases of vCJD pending confirmation of a diagnosis, and the incineration of instruments used on confirmed cases of vCJD. Crucially, early notification of suspected cases is required in order to

facilitate the tracing and recall of blood donations made by individuals who are subsequently found to be infected with vCJD (SEHD, 1999b; NICE, 2006).

The risk of infection through surgery is aggravated by the fact that a patient undergoing surgery will not necessarily be known to be a vCJD infected individual as no specific, reliable test is available to date, although a claim to a notable advance has recently been made in the form of a new test that could be used to routinely test blood donations for vCJD by 2009 (Moss, 2007). Meanwhile, the nature and frequency of surgical procedures of all patients, but particularly of patients who have a high level of donor exposure, should be investigated to examine potential routes of transmission; that is, specific procedures with high risk of infection or high levels of transfusion, to identify individuals who may be at risk. Data such as the study dataset can be used for this purpose: indeed the study dataset has already been used to provide preliminary data on the subject of multiply-transfused patients in the context of concerns over vCJD transmission via blood. Interest in this important area of research is unlikely to diminish as the emergence of vCJD is one of the largest influencing factors on blood donation, transfusion risks and transfusion practice currently contributing to the drive towards safe and effective use of blood components, and although the present study was limited to data for the year 2000 and to a subset of Scottish hospitals, the methods of analysis could be applied to similar national data for a longer time period in the future .

Impact of the ageing demographic of the UK population on red blood cell use

The UK has an ageing population: people are living longer and younger age groups are diminishing. Because changing demographics are expected to have a marked impact on clinical and transfusion practice, the effect on the use of red blood cell transfusion was modelled up to the year 2031 (section 10.6). The findings demonstrated that red blood cell use is expected to increase at a rate higher than the rate of population growth due to the expansion of older age groups, typically over 60 years of age (and particularly for males) who have a higher rate of transfusion than other age groups (Figure 10.5). Indeed, the total population in 2031 is projected to be the same as in the year 2000 but red blood cell use is estimated to increase by 37.8% in that time. The effect was exemplified by total hip replacement procedures that are commonly performed for patients over 60 years of age. The

change in red blood cell use for primary and revision hip replacements was modelled for the whole of Scotland for the year 2031 based on observed rates of transfusion and at a best practice figure described for the study population but not accounting for any changes in the epidemiology of disease, changes in treatment options or developments in prostheses, for example; the latter of which could provide more successful options for long-term primary fixtures thus reducing the need for revision operations and related requirements for blood. The findings indicate that the estimated number of red blood cell units used for total hip replacements in 2000 was 8.4% of the total red blood cell use for Scotland and was predicted to increase to 11.5% of the total red blood cell use for Scotland in 2031 (section 10.4, Table 10.7). Thus, the findings show that the dataset can be employed to predict the effect of demographic change (in the form of an ageing population) on the use of blood in general and specifically for procedures that are common to old age.

There are likely to be numerous opportunities in which the study data and the application of the methods employed in this study can be utilised in the future, further to the applications explored in Chapter 10 and discussed here in section 11.2. Analyses of transfusion recipient survival, donor exposure, practice variation, infection risks and further analysis of the clinical use of blood for epidemiological, research, quality assurance and planning purposes will be highly valued in the context of continuing efforts to make blood transfusion as safe and effective as possible.

11.3. STUDY DATA AND METHODS

The data extracted for the STEP feasibility project, and subsequently used in this PhD study, came from two routine datasets: an inpatient clinical data scheme (linked SMR01/06/GRO, ISD), and a blood bank record system (MAK-Progesa, SNBTS). To evaluate the implications of using these data sources in the development of the present study, the specific strengths and weaknesses of the data, the merits of using routine data in medical research and issues concerning the population represented by the study data are discussed here.

Further, a review of comprehensive, descriptive studies of red blood cell use by clinical case group raised particular methodological issues central to appropriate analysis of the clinical use of blood, highlighting the developments needed in research methods to ensure studies are conducted appropriately and effectively in the future. These factors, namely definition of study population, coding of clinical data and classification of case groups, and the methods used to link blood use to clinical case groups, were considered in the approaches employed for this study.

11.3.1. Strengths of study data and methodology

The transfusion data used in the study was extracted from SNBTS blood banks that utilise the Progesa blood bank computer system. Because the records were obtained from a common, routine reporting system records from different hospitals could easily be combined to form a single source of transfusion data in preparation for further processing. Transfusion records underwent compaction by 24-hour period (using date of transfusion) to create transfusion day records, in order to facilitate later stages of record linkage using date variables. The process was carried out by SNBTS staff as it required specialist knowledge of and access rights to the SNBTS blood bank computer system.

The study included all available transfusion day records of used blood component units for the study population for the year 2000. Even though restricted to one year, the available transfusion data provided a comprehensive resource of information for all blood component

units used in the year for patients included in the study. This meant that the data could be viewed at a patient level rather than being restricted to single transfusion events per patient such as in the study by Mathoulin-Pelissier *et al* (2000). The value of this is illustrated by the case group of haematological conditions for whom all transfusion events within the study period were attributed to the haematological diagnosis making it possible to consider the patient's total transfusion requirements for that period. For certain other patient groups not yet defined the most meaningful study period may be from point of first diagnosis to death: however, a compromise between availability of data and feasibility of analysis must be made.

Clinical (SMR01-CD) data was extracted from a routine database of SMR01 records held by ISD, linked to cancer (SMR06) and death (GRO) records, for all patients whose identities could be linked to a patient identity in the source data of transfusion day records of blood component unit assignments. SMR01 is a data scheme for inpatient and day case records that contain patient demographic and clinical data and data pertaining to individual consultant episodes of hospital care submitted to ISD by hospitals. Issues regarding the large amount of clinical data and the consequences for defining methods are discussed presently (section 11.2.2). First, SMR01 records are generated from information largely drawn from discharge letters and patient case notes by hospital coding staff. The conventions of clinical coding are governed by comprehensive guidelines developed by ISD: these include guidelines on how to resolve queries by encouraging coding staff to consult with the clinicians responsible for the episode of care and subsequent discharge letter. The data contained in SMR01 records undergoes routine quality assurance checks that are carried out by ISD to validate the accuracy of coding practices. Quality assurance checks indicate that SMR01 data variables consistently show a high rate of accuracy for the coding of clinical data by comparing coding information submitted by hospitals with original hospital clinical records, though the level of accuracy have on occasion been below the target level required (ISD, 2004). Further, the completeness of SMR01 records at a given point in time is affected by the promptness of submission of records by hospitals to ISD and could pose a potential cause of data loss. However, in 2004, when data for the year 2000 was extracted for the STEP feasibility study the submission of SMR01 records by relevant hospitals for the study period was complete. The date of death variable was current at the date of data extraction and no subsequent update on the date of death variable was sought during this study as survival analyses were not planned in the present study.

As well as the file of all SMR01-CD records that could be linked to patient identities in the source data of transfusion day records, a file of all SMR01-CD records for the whole of Scotland for the year 2000 was available. This file provided a source from which relevant denominator data could be obtained: for example, number of operations performed, number of patients who underwent specific operations, number of episodes containing specific diagnoses, and number of patients with those specific diagnoses regardless of patients' transfusion status.

Following extraction, transfusion and clinical source data underwent linkage processes at ISD. The first process utilised probability matching of patient identifier variables: by comparing patient identifying information to decide whether or not records relate to the same person a unique number could be attached to records on an individual patient basis. The process of exact matching previously used by ISD for this process missed many true matches due to errors in recording but probability matching employs a highly validated computer algorithm that allows for imperfections in the recording of data (Kendrick & Clarke, 1993; Kendrick, 1997). The variables examined include surname (and its phonetic code to overcome differences in spelling), first initial (and full forename and second initial where available) sex, postcode, date of death (if available), and year, month and day of birth. Other patient identifiers such as hospital case reference number, CHI/UPI[7] number and NHS number are used where available. The assignment of a unique patient identifier to all records was critical to selecting SMR01-CD records for patients with transfusion day records and to the linkage of SMR01-CD and transfusion day records to form the study dataset. Unique patient identifiers also allow for additional record linkage in the future such as to new or additional SMR data schemes or updated GRO death record information.

The sources of routine transfusion and clinical data and the processes of validation and quality assurance of clinical data have been examined and described to evaluate the data used in this study. The data was obtained from datasets that are routinely collected and routinely undergo validation and quality assurance checks. By utilising routine datasets not only is the quality of the data monitored but important savings are made in the time and resources, and indeed funding, that would otherwise be required for data collection. Further,

[7] CHI: Community Health Index number, the national unique number for any health communication related to a patient. UPI: Universal/unique patient identifier

because the data exists in established computer registers there is added benefit in that data input is eliminated and automated linkage and computational processes can be utilised. The role for routine, computerised data sources and automated processing in blood use analyses have been described previously (Titlestad *et al*, 2001 & 2002; Syrjäla *et al*, 2001; Zimmerman *et al*, 19997 & 1998; Lim *et al*, 2004; Stanworth *et al*, 2002).

11.3.2. Weaknesses of study data and methodology

Potential weaknesses of the available data including problems with data variables, the study population and study period, and missing data are discussed next. First, in transfusion day records there was no variable based on direct observation and recording of the number of units infused into, or used by, the patient. The variables for blood component unit measurement contained in extracted transfusion day records were the number of units assigned (that is, reserved and compatibility labelled for a specific patient) and the number of units deassigned (that is, returned to blood bank). Therefore a new variable, termed "used", was computed and consequently, all results relating to blood use are subject to the assumption that the number of units used is equal to the number of units assigned minus units deassigned. The assumption could overestimate blood use in cases where blood component units were assumed to be transfused but were in fact otherwise discarded without record. However, previous validation of this assumption indicates that the estimate is appropriate (Palmer, personal communication);

The study population was defined as all patients with a transfusion day record in an SNBTS blood bank Progesa system and all extracted transfusion day records were retained in the study if they could be linked to SMR01-CD records. However, some of the transfusion day records in the study data carried hospital codes for hospitals that were not expected to be included in the study because they do not utilise the SNBTS/Progesa blood bank system. In the main these represent instances where SNBTS/Progesa blood banks assigned blood component units directly to patients in other hospitals that do not use the same blood bank system, for example, for whom there has been a special request for specially typed units of red blood cells for a patient with red cell antibodies that make it difficult to find compatible

donor red blood cell units. In addition, some instances of unexpected hospital codes may represent patient transfers whereby blood component units were assigned in one location and were transferred with the patient to a different location where the patient was subsequently transfused. The number of units accounted for by these instances is small and has minimal effect on the attribution of transfusion events to clinical case groups.

However, this issue does affect the selection of an appropriate denominator population. The hospital code included in the dataset is the hospital at which the transfusion was given and so for patients whose transfusion day record was generated as a result of a special request or patient transfer a non-SNBTS/Progesa blood bank hospital is reported. Selecting a denominator population based on the hospital codes contained in SMR01-CD records in the study dataset would include all SMR01-CD records for the year 2000 for those hospitals for which a special request for blood or patient transfer had occurred, whereas the majority of these hospitals' transfusion data is not included in the study. Therefore, by overestimating the size of the denominator population, blood component use per episode of care, patient, or operation would be underestimated. Thus, the issue was addressed by selecting a denominator population for all hospitals in the transfusion day records source data excluding those hospitals for which blood was not supplied by an SNBTS/Progesa blood bank other than for special requests or patient transfers. That is, the hospitals selected represent only hospitals for which all blood banking (and so patient specific blood component assignments) is performed by an SNBTS/Progesa blood bank. Therefore, the denominator data selected for the study underestimates the total number of procedures and diagnoses for the study population because it excludes some clinical data relevant to the study dataset (that is, the data for patients transfused at non-SNBTS/Progesa hospitals). However, only a small number of transfusion and clinical records with such excluded hospital codes appear in the study dataset.

The data shows that the red cell using surgical procedures defined in the study tend to be associated with a single inpatient episode and any further, related clinical care tends to be at the same hospital as that at which the procedure was performed. Therefore, for analyses of blood attributed to surgical case groups the denominator population was largely appropriate. However, for haematological conditions, patients may be diagnosed and receive treatment at several different hospitals over a protracted period of time. The

distribution of patients between the haematological diagnoses varies between the denominator data and the study data because of cases where the patient was initially diagnosed and treated (transfused) for a haematological condition and where the patient was subsequently treated (transfused) for that or a related haematological condition at a different location, and depending on the progression of disease of those conditions if any was reported. The issue of selecting a representative denominator population would have been avoided had the transfusion day records that carried a non-SNBTS/Progesa blood bank hospital code been removed from the study dataset at the start of the study and is a reminder of the benefit in studying a whole population's use of blood.

Another potential weakness in the scope of the study was the study period. Firstly, the data was for the year 2000 which, at the time of the present study, means that the data is seven years out of date. It is acknowledged that changes in clinical and transfusion practices that could affect the rules for blood attribution and subsequent interpretation of the findings for blood use by clinical case group are likely to have occurred during this time. This is an issue integral to the study being a pilot study and one that has been addressed by the subsequent creation of the Scottish Transfusion Epidemiology Database (STED) (section 11.5) which provides up to date blood use data for Scotland. Further, the one-year period provided a cross-sectional observation of patients' clinical events and would be expected to include a case mix of a range of stages and severity of disease and surgical complexities. Any fixed time frame that defines a window of available data means that information at the very start and very end of the period cannot be properly assessed unless specific, additional records are sought, because interpretation may be dependent on transfusion or clinical data in previous or subsequent records not included in the study. This is not a problem of the data per se, rather is an issue of the methodological approach adopted. The so called "edge effect" has less impact on analysis and interpretation of available data the longer that the continuous time frame of study is. In the review of published evidence of comprehensive, descriptive studies of clinical blood use, the study period ranged from two weeks to six years, with the most common length of study being one year (section 3.4). Again, as has been previously acknowledged, a compromise has to be made between comprehensive data collection and feasibility of collection and analysis.

A further potential weakness of the available clinical data is that it does not include information for outpatients and so the study dataset can not be used to report on blood use by clinical reason for outpatient transfusions. Outpatient data is recorded in a separate data scheme designated SMR00 that was not available for linkage to SMR01 records when the study data was extracted. The study data also lacks maternal, neonatal, and birth data because SMR02 (maternal) and SMR11 (neonatal, now Scottish Birth Record) data schemes could not be linked at the time the study data was extracted. Transfusion events that could have been linked with one of these other data schemes could have been missed out of the study dataset if the patient did not also have an SMR01 record in the study year. Transfusion day records in the study dataset that could have been linked with one of these other data schemes and were linked to patient identities with SMR01 records may have been more appropriately described by the non-SMR01 data either in place of or in addition to the link with clinical indications identified within the SMR01 records.

In summary, potential weaknesses of the source data include the lack of a variable for transfused units, the inclusion of some specific, non-SNBTS/Progesa blood bank transfusion day records and the subsequent impact on defining a denominator population, the scope of the study period, and the lack of record linkage to additional Scottish Morbidity Record data schemes. Notably, a weakness of the source data is that in neither SMR01-CD records nor transfusion day records is the clinical reason for transfusion specifically recorded; this issue is central to the requirement for the definition of blood attribution rules and clinical case groups, which are discussed next (section 11.3.3). Whilst acknowledging the limitations posed by these issues, the source data of transfusion day records and SMR01-CD records was considered to have been appropriately selected and to have provided useful and validated data for the study. Further, subsequent methods were devised with consideration for potential approaches to address these limitations.

11.3.3. Study dataset development: Records not included in study

As has been described and discussed elsewhere, the study dataset was created by linking patient identities in the source data, that is, transfusion day records of unit assignments and SMR01-CD records, and selecting for transfusion day records of units used (section 5.2). Some transfusion day records of unit assignments could not be linked to a patient identity with an SMR01-CD record in the year 2000, a subset of which are transfusion day records of units used. Transfusion day records that cannot be linked to SMR01-CD records are likely to occur because the hospital activity of the transfused patient was recorded in an alternative SMR data scheme, for example, maternal (SMR02), neonatal (SMR11) and outpatient (SMR00) records that were not available for study at the time the data was extracted for the STEP feasibility study. 5.7% of the total number of transfusion day records of units assigned in the source data was not included in the study dataset because they could not be linked with SMR01-CD records for the year 2000. The implication is that 3.6% of red blood cell units used could not be described by clinical case group and the reasons for maternal, neonatal or outpatient transfusions could not be elucidated. Record linkage with these data schemes is recommended for future analyses of this sort.

Further, the study dataset was limited to transfusion day records of units used and so SMR01-CD records for patients for whom blood was assigned but who were not subsequently transfused were not included in the study dataset. However, these records are available for future analysis, for making estimate of total blood supply requirements, for example.

The small number of transfusion day records of units used that cannot be linked to SMR01-CD records and the fact that reasonable explanations can be provided for this indicate that low levels of data loss were encountered between data extraction and record linkage, thereby providing what can reasonably be considered to be a comprehensive study dataset for the relevant study population and period.

11.3.4. Methodological challenges relating to dataset development and the attribution of blood to appropriate clinical case groups

The strengths and weaknesses of the source data were discussed previously (section 11.3.2) and are referred to here in the context of the methodology that was devised and employed to create and analyse the study dataset. Basic characteristics of transfused patients and blood component use were described directly from the transfusion data in the study dataset. Further to this, a principal objective of the study was to identify a means of classifying and quantifying blood component use by clinical case group. The fundamental issue with this aim was that the clinical indication or reason that can explain the patient's requirement for a blood transfusion was not recorded in the available data; indeed it is rarely explicitly recorded in transfusion records or patients' case notes not just in Scotland but in other countries in which this kind of analysis has been attempted (Sirchia *et* al, 1994). Consequently, a major part of this study was to devise methods that could be used to attribute used blood component units to an appropriate reason for transfusion thus enabling blood use by clinical case group to be described. The issues encountered and the consequences for the methods employed in this study are discussed here.

Two notable challenges were the multiplicity of clinical and transfusion records per patient during the study period and how to utilise the large amount of clinical data contained in the SMR01-CD records; these are discussed next in the context of defining the blood attribution rules.

The first issue with the existence of multiple transfusion and SMR01-CD records for many patients was concerned with the handling and management of the data. In order that all potential relationships between clinical data and blood component use could be examined, every SMR01-CD record had to be linked in some way to every transfusion day record on a patient by patient basis. To facilitate this, the file of SMR01-CD records was restructured so that all records for each patient were compacted into a single, complex record representing the patient's available SMR01-CD history for the year 2000. Restructuring transfusion day records in this way resulted in the multiplication of blood units which, in the initial trials, caused difficulties in enumerating actual units attributed to clinical case group. The resolution of this problem by restructuring SMR01-CD records and not transfusion day records was a marked advance in terms of the mechanics of data handling. Consequently,

the study dataset allowed for all possible relationships between transfusion day records and SMR01-CD records to be examined in a format that would facilitate subsequent flexibility of analyses of blood use.

In order that an inference could be made as to which clinical code within SMR01-CD records was the relevant clinical data to which blood use should be attributed, blood attribution rules were devised. The first task undertaken to relate blood use to clinical case groups was to define date rules that linked transfusion day records with SMR01-CD with temporal relevance. The date rule developed to link transfusion day records with a specific SMR01 episode of surgical intervention defined a relationship between the date of blood component assignment and dates in the clinical record pertaining to the episode of clinical care (date of admission and date of discharge). A wider window of attribution was considered for haematological diagnoses: all transfusion day records for the year 2000 of patients with any instance of a relevant diagnosis were attributed to haematological case groups. The date rules were defined using clinical judgement about the likely temporal relationship between blood assignment and use in the context of current transfusion and clinical practices in Scotland. The date rules employed in future studies of this sort should consider relevant practices to ensure that appropriate attribution of transfusion day records to SMR01-CD records is made. Changes to the date rules may require additional clinical experience to be incorporated, as well as adjustments to account for the effects of changes in transfusion practice and clinical practice over time.

The second requirement of the blood attribution rules was to link transfusion day records with clinical case groups identifiable within appropriately linked SMR01-CD records. The conventions used to code clinical data in SMR01 records (as defined by ISD) were examined to gain an understanding of the availability and construction of the data coded in the procedural (OPCS-4) and diagnostic (ICD-10) variables. An inference had to be made about the clinical event or condition that should be considered as the likely reason for transfusion: clinical case groups could be coded in any of the four procedure variables and six diagnostic variables (intra-episode competition, Figure 5.4a). Where the surgical date rule linked more than one SMR01-CD containing a red cell using procedure to a transfusion day record or where a haematological patient had more than one SMR01-CD containing a haematological diagnosis in the year a further decision had to be made to define the relevant case group that

represented the overall likely reason for transfusion (inter-episode competition, Figure 5.4b). The issue of multiple clinical variables giving rise to intra- and inter-episode competition was one of the largest factors affecting the definition of clinical case groups and how blood use was attributed to clinical case groups. Because the clinical coding conventions guide the coding of clinical data by importance or priority, the issues of competition were resolved by accepting the first red cell using procedure or haematological condition occurring chronologically, and within SMR01-CD records, as the case group to which blood use was attributed. The impact of this on the findings of blood use by clinical case group depends on the likelihood of major surgical events or chronic conditions being recorded together; the specific findings for this study are described next.

The combinations of clinical case groups for instances of competition were reported alongside the overall results for surgical and haematological red blood cell in order to give a more complete picture of the clinical reasons that can be related to blood use (Chapters 8 and 9). All instances of competition for the attribution of blood in this study are between two red cell using procedures or between two haematological diagnoses. Overall there were few instances when using the surgical blood attribution rule that red blood cell use could be attributed to more than one of the defined surgical procedures (and in no case more than two): 26.0% of transfusion day records were linked to one SMR01-CD record containing a red cell using procedure; 0.2% could be linked to two SMR01-CD records containing a red cell using procedure. 73.8% of transfusion day records of red blood cell use (71.1% RBC units used) could not be linked by the surgical blood attribution rule to any SMR01-CD records. In some instances the two competing red cell using procedures were the same, that is, a red cell using procedure was recorded in both of the two SMR01-CD records that satisfied the temporal relationship for the surgical blood attribution rule. In some instances the two competing red cell using procedures were related by specialty of anatomical site. The competition was therefore potentially illusionary and could be considered as resolvable in these cases. In only a small number of instances were the two competing procedures different and not related in an obvious way, and therefore considered to be irresolvable. Because of the small scale of the problem it had minimal impact on the findings.

Furthermore, the cases of competing haematological conditions reflect clinically relevant changes in diagnosis likely due to clinical progression and presentation of disease. The

initial condition may evolve to another condition and complications due to the primary condition are common in these diseases, therefore, competing reasons for transfusion are not unexpected for haematological patients. Because pre-malignant conditions were included as a haematological case group the assumption that relates blood use to the first haematological case group within and between competing SMR01-CD records may cause the amount of blood attributed to pre-malignant conditions to be overestimated: the pre-malignant condition is more likely to be diagnosed first and so blood is attributed to that rather than any subsequent diagnosis of haematological malignancy. This issue supports the underlying issue regarding what constitutes the most likely reason for transfusion and highlights again that the rules developed for this study make inferences about the appropriate attribution of blood use to clinical case groups as well as being based on decisions about the definition of haematological case groups considered to be appropriate for inclusion in this study. Concerns regarding the poor or inaccurate classification of haematological malignancies in clinical practice and research were raised in section 11.2.3 (Cartwright, Gilman, & Gurney, 1999).

Had competing case groups, particularly competing red cell using procedures, been frequently identified, adjustments to the ways in which clinical data was summarised and patients were classified would have been necessary. Because only a few instances of irresolvable competition were identified, because the assumption reflects the inherent order of priority or importance that is conventionally given to clinical data at the point at which SMR01 records are coded, and because it can be argued to be logical, clinically, to relate blood use to the first relevant case group, the proposed assumption was accepted as being appropriate for this study. This is an example of how investigation of clinical coding played an integral part in the validation of the methods that were employed for the attribution of blood to clinical case group in this study.

Finally, the clinical case groups employed in this study are representative of the data coded in a single clinical variable: the detail of clinical data across other variables is disregarded and the decisions made in each case affect subsequent analyses. However, the clinical data had to be summarised by some method and this step was considered to be appropriate and useful for facilitating further analysis although it is acknowledged that alternative approaches and definitions could be used in other studies of this sort. The full clinical data

was retained in the study dataset and could be referred to if there was a data query or particular interest regarding a particular clinical combination of procedures and/or diagnoses, and meaning that alternative case groups could be included should that be a requirement of future analyses.

In conclusion, the availability of multiple transfusion and clinical records and the large amount of clinical data for many patients in the study dataset meant that methods had to be devised to address intra-episode competition (when ascribing clinical case groups to SMR01-CD records) and inter-episode competition (when multiple SMR01-CD records could be linked to a transfusion day record) so that blood could be attributed to appropriate clinical case groups. A sound understanding of the data as well as clinical input was required in order to define appropriate blood attribution rules but it is acknowledged that the methods were based on a number of assumptions, specifically relating to the list of red cell using procedures, the date rules and the resolution of competition. Due to the variation of the clinical nature of the inpatient study population, and the lack of a recorded clinical indication for transfusion, it is acknowledged that an inference was made to define the reason for transfusion and that the study was unable to determine absolutely the reason for transfusion. All rules, methods and assumptions were made in with a sound understanding of the nature and structure of the clinical data in SMR01-CD records in combination with clinical advice, and an awareness of the limitations of the approach. However, potential areas for future developments of the methodology exist and are discussed in section 11.5.

11.3.5. Study population: representation of blood component use in Scotland

In order to quantify how much blood a population such as Scotland needs, it is desirable to collect data that represents the complete picture of transfusion activity for the whole population for the specified time period. However, the data utilised in the study had been collected for the STEP feasibility study and was limited to one year's transfusion data from SNBTS/Progesa blood banks. The data from this common and routinely employed reporting system was readily accessible by Scottish National Blood Transfusion Service staff. However, as has been described, the SNBTS/Progesa blood bank system was not used by all

blood banks in Scotland in the year 2000 and hence the extracted transfusion data represents only a proportion of the hospitals that were supplied with blood by SNBTS in the year 2000.

The study population could not be calculated as a proportion of patients in the population because data was not available to quantify the population served by individual hospitals. The population of each health board area was available but not all hospitals in a health board area were included in the study data. Similarly, it was considered inappropriate to describe the study population in terms of the proportion of transfusion day records because an appropriate denominator could not be identified or quantified; nor in terms of SMR01-CD records because they do not represent a measure of transfusion practice and further, due to variations in hospital type, specialties provided and patient case mix make an appropriate denominator difficult to quantify.

Because of these reasons the proportion of the Scottish population represented by the transfusion data was calculated in terms of the proportion of red blood cell units supplied by SNBTS during the study year. Red blood cell supply data for the year 2000 for the blood banks included in the study and the total supplied to the whole of Scotland was available from SNBTS records: records of total issues by depot, total issues per period and summaries of units assumed to have been transfused by institution were available for individual hospitals. However, the data was difficult to interpret and understanding was only made possible due to the work carried out for the development of Surgical Blood Use reports for the Better Blood Transfusion Programme (Stewart, personal communication). Using this data it was possible to estimate that the study population represented 38% of the Scottish supply of red blood cell units in the year 2000. However, this estimation makes an assumption about transfusion practice in Scotland similar to the issue of variation in clinical practice described above; that is, the estimate relies on the assumption that that the use of red blood cells was the same for the included in and excluded subgroups of the population. Subsequent analysis using the Scottish Transfusion Epidemiology Database, in which data for almost all of Scotland is included, suggests that red cell use per head of population is higher in the west of the country (section 11.4).

11.3.6. Future opportunities with new and additional data

It was acknowledged from the start of the study that due to the partial nature of the blood bank data then available this pilot study would be able to make estimates only of blood use for the whole population based on the assumption of uniform use. The limitations of the study data provide scope for developments for future analyses of clinical blood use. For example, because the data was for one year it is difficult to describe the clinical use of blood in the broader context of patients' lives. Also, because the available source of transfusion data restricted the study population to a proportion of the Scottish population, it was not possible to explore the question of a whole population's use of, or need for blood. The availability of transfusion and clinical data that represents the whole population for a specified study period would mean that movements of blood between institutions such as by special blood type requests, or movements of blood and patients such as by patient transfer between clinical facilities would not affect the population included in the study data and that the denominator population could be easily defined. Further, the data would represent the entire case mix of patients for the whole country and would eliminate the need to make assumptions about the transfusion and clinical practice of a proportion of the country as was done in this study. Indeed, preliminary evidence indicates that blood use does vary in Scotland depending on the provision of medical services, health status and deprivation (Stewart, personal communication).

In conclusion, the dataset created in the present study provided a suitable resource for this pilot study but further development of the project would benefit from the availability of clinical and transfusion data that relates to the whole population, can be linked with data for additional years, and is recent data that reflects current transfusion and clinical practices. The Scottish Transfusion Epidemiology Database was created subsequent to the methods of dataset creation in the present study and is a potential resource of comprehensive and continuous, national data (section 11.4).

11.4. BETTER BLOOD TRANSFUSION PROGRAMME REPORTING SYSTEM

The present study represents an essential phase of research that created a study dataset and devised methods with which to link transfusion and clinical events in order to describe blood use by clinical case group. In this way, the present study has directly contributed to the creation of the Scottish Transfusion Epidemiology Database (STED). The Better Blood Transfusion Programme (BBTP) has undertaken to collect data similar to the present study's dataset for the whole of Scotland on a continuous, routine and automated basis. The methods employed in this present study are now being applied to the Scottish Transfusion Epidemiology Database and the results for blood use attributed to procedural case groups are being packaged as standard Surgical Blood Use reports.

The format and content of Surgical Blood Use reports were developed by BBTP in collaboration with clinical consultation and have been rolled out across Scotland for all providers of blood use data. Initially coverage was low but extensive work was carried out to encourage participation and to facilitate data sharing in order that all institutions in Scotland that use blood are included, although to date coverage is still not 100% complete. Institutions are required to submit blood use data on an annual basis; a secure, web-enabled data transfer facility is available for this. The data is held in a data warehouse (the Better Blood Universe) at ISD and feeds a web-based, end-user reporting system in hospitals.

Table 11.4 Variables in data warehouse used in surgical blood use reporting (Appendix A.3: excerpt from example Surgical Blood Use report)

Variables reported for surgical blood use
Number of patients
Number of patients at risk of transfusion (blood component assigned)
Number of patients transfused (blood component used)
Number of procedures
Number of procedures transfused †
Blood components used per patient (and patient transfused)
Blood components used per procedure (and procedure transfused)

*Recorded as confirmed transfused via the "Bag and tag" traceability system (not available for PhD data). † Cannot be quantified automatically for PhD study where patients have more than one blood using procedure.

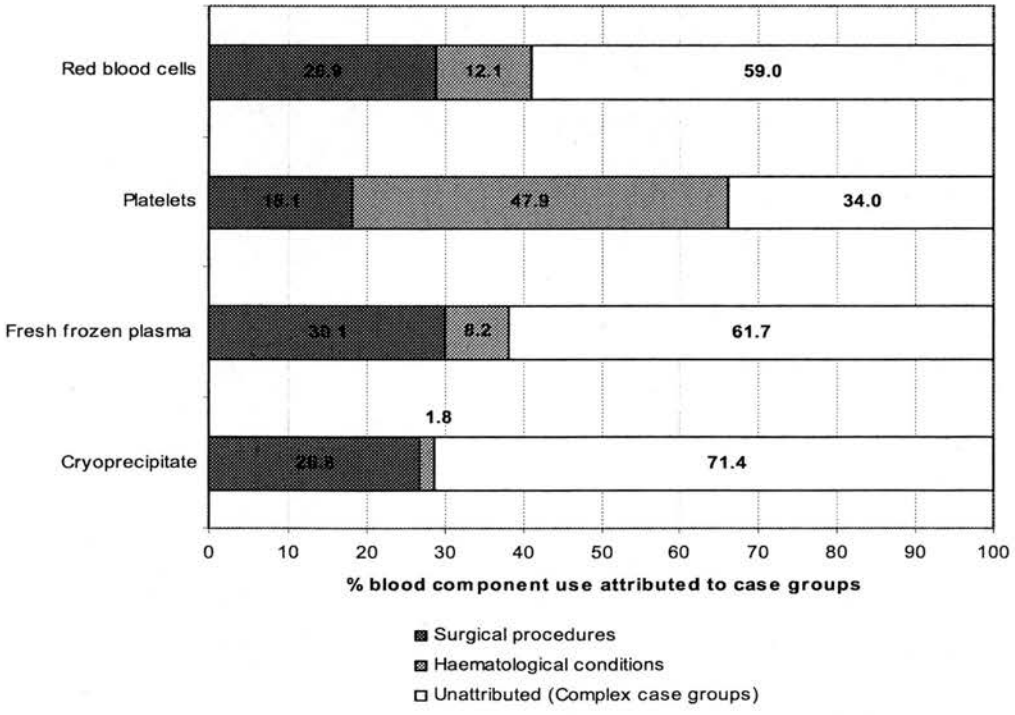
Surgical Blood Use reports are available at a clinician, hospital, regional and national level, and organisational and temporal comparative data can be provided (Appendix A.3) (Stewart, personal communication). The data is linked with inpatient and day case (SMR01), cancer (SMR06) and death (GRO) records and can be linked with maternal (SMR02), neonatal (SMR11), outpatient (SMR00) and Ward Watcher clinical records if, or indeed when, future developments facilitate such record linkage

Ongoing development of STED and available blood use reports has also preliminarily addressed diagnostic blood use, like the haematological conditions described for this study, and considers additional patient case groups that have as yet not been fully described or incorporated into blood use reports. The data warehouse and user requirements are continually updated in response to project developments.

11.5. ALTERNATIVE APPROACHES AND FUTURE WORK

The study aimed to describe the clinical use of blood: this aim was achieved to the extent that 29% of red blood cell units were attributed to surgical case groups and 12% of red blood cell units were attributed to haematological case groups specifically developed for this study. Therefore 59% of red blood cell use has not been attributed to an underlying clinical reason that can explain the use of blood as defined in this present study (Figure 11.1). It has been acknowledged here that the nature of the procedural and haematological rules developed for the study mean that the reason for transfusion is inferred from the clinical data in available SMR01-CD records and that alternative relationships could potentially be inferred if those rules were altered. A quality of the study dataset is that alternative or additional blood attribution rules of a similar format to those devised for the present study could be applied to report on blood use by clinical case group in the future.

Figure 11.1 Classification of blood component use by specified clinical case groups showing units not attributed to clinical case groups in this study



Note1: Cross-reference Figure 9.3

Thus there are two areas that could be targeted for future development. One, improvements could be made to the existing blood attribution rules to reflect changes in clinical and transfusion practice. Two, clinical case groups could be defined in addition to the red cell using procedure and haematological case groups defined in the present study in order to describe the clinical reason for the use of red blood cell units so far not attributed in this study. Factors such as the type of surgeries performed, new diseases and combinations of procedures or clinical conditions should be taken into account in the future. Suggested developments in these areas are discussed next.

11.5.1. Alternative approaches to blood attribution rules

The two aspects to the rules developed for the attribution of blood to clinical case groups are the date relationships between transfusion event and relevant period of clinical care and the clinical case groups defined as likely users of blood.

The surgical blood attribution rule referred to instances where it was considered sensible to view the data from a procedural perspective for which a small timeframe of association was used to link transfusion events to major elective procedures that were likely to require a red blood cell transfusion: for example, coronary artery bypass graft operations and hip replacement procedures. The haematological blood attribution rule referred to instances where it was considered useful to view the data from a diagnostic perspective for chronic haematological conditions that are likely to require multiple transfusions over a protracted timeframe (a year in the case of this study). The date rules were defined for the context of current transfusion and clinical practices using clinical input but could be adapted to reflect changes in treatment protocols and prescribing practices in the future. Changes could affect the temporal relationship between blood assignment and the relevant period of clinical care during which blood components may potentially be used, or might affect the approach employed to resolve instances of competition between case groups. Iterative, data-driven approaches to defining timeframes within which a specified proportion of blood assignments are made for different clinical case groups could be utilised but whatever approach is adopted, the date rules developed should always have clinical relevance to the practices of prescribing and treatment with transfusion.

The red cell using procedures and haematological diagnoses included in the study were experientially defined but there is scope to employ a data-driven approach. By exploring the frequency with which procedures or diagnoses are coded in the primary procedural or diagnostic variables in SMR01-CD records and can be linked (by whatever temporal rule is employed) with transfusion events, additional or alternative red cell using procedures or diagnoses that are frequently coded clinical events that can be linked to transfusion events might be identified. However, as with alternative definitions for date rules, the methods employed to define relevant clinical case groups cannot be purely data-driven and will always require an element of clinical input to eliminate procedures and diagnoses that, while identified by data-driven approaches, have no clinical relevance for inclusion.

Therefore, changes to the date rules to reflect changes in transfusion practise and changes to the clinical case groups that define the likely reasons for transfusion should be considered and explored in order that the most full and accurate description of the use of blood by clinical case group is made in the future. Additional clinical case groups and alternative perspectives for defining the clinical reason for transfusion are described next (section 11.5.2).

11.5.2. Additional approaches to describing blood use for transfusion events not already attributed to clinical case groups

There are numerous opportunities to revise or add to the clinical case groups that could be related to transfusion events in future analyses. Methods to identify additional red cell using procedures and diagnostic conditions were discussed briefly in the previous section (11.5.1). Specifically, other chronic medical conditions for which frequent blood transfusions are the usual method of treatment could be added as the use of blood for medical conditions is frequently reported as being on the increase. Some of the diagnostic areas that might be considered can be identified from previous reports and include oncology and gastroenterology (Table 11.5). Where medical conditions have potential to be common comorbidities of conditions already described by the haematological case groups or by new diagnostic case groups, separate case groups should be defined that allow for the analysis of any overlap in blood that can be attributed to more than one diagnostic case group, or

indeed to both diagnostic and procedural case groups. Competition within and between the red cell using procedures and haematological conditions defined for this study has been explored; further competition between the specifically defined red cell using procedures in this study and other surgical procedures not yet classified by case group in this study might also occur and require investigation.

In general, the 15,475 transfusion events (58.9% of total in study dataset) that are thus far not attributed to a clinical case group in the present study represent patients with multiple inpatient admissions (average SMR01-CD records per patient 4.45, SD 3.98) and complex clinical histories that encompass both surgical events and multiple comorbidities. In many cases the relationship between clinical information is not easily revealed, is not amenable to automated analysis and requires case-by-case clinical judgement. Furthermore, as for the whole study dataset, many of the patients are elderly (mode ageband 70-79 years, 59.1% of patients "not attributed" aged over 65 years). The combinations of procedures and diagnoses for these so called complex patients might in the future be viewed in various ways: as specific combinations of related procedures and diagnoses, or as particular cohorts of patients of interest from a public health perspective. The various approaches that could be explored to identify additional, appropriate case are described here.

The approach of defining case groups using specific combinations of related procedures and diagnoses is perhaps best described by an example: gastroenterology has been identified as an area of significant blood use but the underlying need for transfusion is not easily distinguished (Wallis, Wells & Chapman, 2006; Friedman, Burns & Schork, 1979; Cook & Epps, 1991; Chiavetta *et al*, 1996; Mathoulin-Pelissier *et al*, 2000; Lim *et al*, 2004). Some gastrointestinal procedures are already included in the red cell using procedure case groups identified for this study (open operations on oesophagus, excision of colon, excision of rectum) but other related diagnoses (for example, malignant neoplasm of gastrointestinal tract, peptic ulcer, oesophageal varices, Crohn's disease, ulcerative colitis and gastrointestinal haemorrhage) are also likely to be important in identifying gastrointestinal patients at risk of transfusion. Specifically, gastrointestinal endoscopy may prove to be an important marker for identifying blood users. Although the endoscopy in itself cannot be described as the reason for transfusion it is very common for bleeding patients to have an

endoscopy both to identify the source of bleeding and to arrest the bleeding. It also follows that gastrointestinal bleeding often necessitates transfusion.

Endoscopies are included in a list of supplementary procedures that were defined during the study but have as yet not been utilised in analyses (Table 11.6). Supplementary procedures were defined in the course of this study in an attempt to identify procedures that, while not primary clinical reasons that necessitate transfusion, instead represent procedures that may prove to be useful markers for indicating potential blood using clinical case groups. The frequency of supplementary procedure codes in SMR01-CD records, and the diagnoses and procedures with which they are coded in combination could provide useful information for the development of gastrointestinal and other complex clinical case groups. The use of supplementary procedures may be limited by under-reporting of these procedures due to the convention for clinical coding in SMR01-CD that states that diagnostic procedures should be coded only after therapeutic procedures (ISD, online). Endoscopy use can be both diagnostic and therapeutic: it is not clear exactly how this is defined by coders, but where ambiguity is encountered guidelines require coders to seek clarification from the clinician responsible for the episode of care.

Table 11.6 OPCS-4 fields that contain procedure codes classified as "supplementary"

Supplementary Procedure	Number of times coded in variable:				Op1/ Total
	OP1	OP2	OP3	OP4	
Endoscopic operations on kidney	5	0	0	0	100.0%
Chemotherapy	5,431	278	103	41	92.8%
Endoscopic operations on prostate	77	7	4	0	87.5%
Endoscopy of upper gastrointestinal tract	2,494	487	141	35	79.0%
Endoscopic operations on bladder	472	100	28	14	76.9%
Endoscopic operations on oesophagus	183	62	25	6	66.3%
Blood transfusion	3,929	1,385	508	198	65.3%
Endoscopic operations on colon	919	388	90	29	64.4%
Compensation for renal failure	428	203	40	17	62.2%
Endoscopy of lower respiratory tract	119	26	53	11	56.9%
Other operations on unspecified organ	2,199	1,404	778	439	45.6%

The supplementary procedures investigation identified a total of 6,020 instances of coding for "blood transfusions" in the SMR01-CD records included in the study dataset. Blood transfusion (OPCS-4 X32-X33) includes transfusion of red blood cells and platelets, neonatal exchanges and other and unspecified blood transfusions. The infusion of plasma, coagulation factors and serum (OPCS-4 X34) was not included. As the study dataset represents 11,994 patients who can be linked to 26,269 transfusion day records of units used (25,315 of which are transfusion day records of red blood cell or platelet use), it is evident that blood transfusion was under-reported in SMR01-CD records available for study in 2000.

The complexities of gastrointestinal medicine illustrate the requirement to identify common combinations of related procedures, diagnoses and appropriate supplementary procedures in order to define appropriate clinical case groups. The following approach is more general in that it could be used to identify cohorts of patients, such as could be easily defined by medical specialty or other cohorts of interest from a public health perspective. SMR01-CD records can be viewed at a patient level, rather than on a record by record basis, as exemplified by the haematological conditions described in this study. This approach would be useful where individual SMR01-CD records do not contain information that could be identified as a likely reason for blood use, but where aggregating information from multiple SMR01-CD records provides an overall picture of the patient's medical conditions and clinical needs. This approach could also be used to address the argument as to which specific aspect of clinical data should be linked to the transfusion. That is, it may render unnecessary the decision as to whether the blood transfusion was due to a procedure or the initial underlying condition that made that procedure necessary. Examples might include cohorts of patients with alcoholic liver disease, colorectal cancer, chronic renal disease, and diseases of old age. These general, patient based approaches may be useful in epidemiological research, high-level reporting contexts but might be less useful to individual clinicians, particularly surgeons, and in specific resource planning contexts.

Finally clinicians with an interest in a particular area of medicine or transfusion practice are also able to describe potential procedure- or diagnosis-specific case groups. Clinicians' specialist knowledge can be used to define specific case groups to identify patients to whom the clinician can relate, thus improving the relevance of and aiding the interpretation of blood use reports. In the early stages of this present study clinical input and an awareness of

clinical requirements was gained from opportunities such as this, especially for oncology and gastroenterology. This approach could be utilised further, either to inform the definition of clinical case groups in general, or to develop specialist case groups if required in the future.

11.6. CONCLUSION

The aim of this study was to explore the feasibility of analysing the clinical use of blood for Scottish hospitals by means of linking records of transfusion and clinical data. The creation of the study dataset has demonstrated that record linkage of routine data is feasible. By defining specific clinical case groups and by devising novel rules for the attribution of transfusion events to clinical case groups, automated analysis of routine data to describe blood component use has been demonstrated. The study reports unique findings for blood component use for Scotland, and specifically by novel clinical case groups. Furthermore, it has been demonstrated that the study data can be used in additional applications to answer a range of other questions about the clinical use of blood.

The limitations of this study in terms of the study population being a subset of Scottish hospitals and the study period being some years past, can be resolved by applying the study's methods to more recent, routine and national data. This study has contributed directly to the recent development of the Scottish Transfusion Epidemiology Database (STED), in which, to date, the representation of red blood cell use for the whole of Scotland is almost complete, and data is available for a continuous period of time from 2002.

Given the complexities of some clinical cases and the necessary judgements as to the actual reason for blood component use, further work is warranted in order to facilitate comprehensive analyses of blood use by clinical case group in the future. One, there is a requirement to define additional, appropriate clinical case groups for the classification of transfusion events, considering the often complex relationships coded within clinical data, using definitions that are internationally recognised and comparable, and considering changes in the epidemiology of disease. Two, there is a requirement to revise the blood attribution rules, taking into consideration future changes in transfusion practice. Further developments with regards to clinical case groups and blood attribution rules should be devised and validated for STED data rather than for the present study dataset.

Transfusion practice faces mounting pressures on the balance of supply versus demand and therefore it is valuable that the study dataset can be utilised to explore and quantify the use

of blood components in response to potential changes in factors affecting transfusion practice. In this study a novel concept of best practice transfusion targets and the use of an alternative intervention, intra-operative cell salvage, were shown to result in encouraging savings in orthopaedics and cardiac surgery, areas of high red blood cell use blood. In particular, current concerns regarding vCJD infection affecting the supply of blood, and the predicted marked effect of the ageing Scottish population on the future demand for blood, alert to the need to consider the development and implementation of blood conservation strategies.

The appropriate use of blood is paramount: initial blood loss must be minimised to reduce the need for allogeneic transfusion, the decision to transfuse should be made considering the balance of benefit versus risk, and a safe and effective replacement for blood should be readily available when required. Thus, there is a need for an appropriate evidence base for the efficacy of blood conservation strategies, such as specific transfusion protocols and alternative interventions, in parallel with an ongoing requirement for monitoring the use of blood, particularly by clinical reason for transfusion and using appropriate and comparable methods, in order to facilitate the safe and effective use of blood in an ever more resource-constrained environment. This research has demonstrated the feasibility and value of this novel approach.

APPENDICES

APPENDIX 1.

Table A.1 Hospitals included and not included in study and denominator datasets

Hospital	Number of SMR01-CD records	Number of TDRs	Study dataset[8]	Denominator data[8]
Hospitals included in study dataset and denominator data				
Edinburgh Royal Infirmary (old)	67,673	7,025	Y	Y
Aberdeen Royal Infirmary	77,609	6,444	Y	Y
Ninewells Hospital	63,249	5,901	Y	Y
Raigmore Hospital	35,565	2,311	Y	Y
RHSC (Edinburgh)	13,610	1,074	Y	Y
Woodend General Hospital	7,246	1,012	Y	Y
Princess Margaret Rose Hospital	3,590	448	Y	Y
Liberton Hospital	898	146	Y	Y
Royal Victoria Hospital (Dundee)	1,037	141	Y	Y
Royal Aberdeen Children's Hospital	8,028	129	Y	Y
Roodlands General Hospital	2,386	83	Y	Y
Kings Cross Hospital	2,454	81	Y	Y
Chalmers Hospital (Edinburgh)	483	76	Y	Y
Dr Gray's Hospital	13,447	55	Y	Y
City Hospital	4,529	44	Y	Y
Astley Ainslie Hospital	826	23	Y	Y
Hospitals included in study dataset				
St John's Hospital At Howden	33,842	91	Y	N
Perth Royal Infirmary	21,637	88	Y	N
Western General Hospital (Edinburgh)	59,068	67	Y	N
Aberdeen Maternity Hospital	70	44	Y	N
Portree Hospital	388	33	Y	N
Mackinnon Memorial Hospital	1,168	31	Y	N
Tor-Na-Dee Hospital	1,067	31	Y	N
Roxburghe House, Tor-Na-Dee Hospital	416	30	Y	N
Town and County Hospital Nairn	361	22	Y	N
Ross Memorial Hospital	466	21	Y	N
Fraserburgh Hospital	677	20	Y	N
Belford Hospital	3,616	19	Y	Y
Stracathro Hospital	8,522	17	Y	N
Lawson Memorial Hospital	1,181	15	Y	N
Turner Memorial Hospital	306	13	Y	N

[8] Y=Yes, N=No

Hospital	Number of SMR01-CD records	Number of TDRs	Study dataset	Denominator data
Hospitals included in study dataset (continued)				
Jubilee Hospital	692	12	Y	N
Chalmers Hospital (Banff)	816	9	Y	N
Inverurie Hospital	297	6	Y	N
Turriff Cottage Hospital	294	6	Y	N
Royal Northern Infirmary	379	3	Y	N
Stephen Cottage Hospital	95	2	Y	N
Caithness General Hospital, Wick	4,606	1	Y	N
Royal Victoria Hospital (Edinburgh)	1,541	1	Y	N
Peterhead Community Hospital	729	1	Y	N
Ashludie Hospital	422	1	Y	N
Arbroath Infirmary	371	1	Y	N
Dunbar Hospital, Thurso	304	1	Y	N
Spynie Hospital, Elgin	232	1	Y	N
Ian Charles Hospital	218	1	Y	N
Insch & District War Memorial Hospital	208	1	Y	N
Seafield Hospital	179	1	Y	N
Edington Cottage Hospital	39	1	Y	N
Hospitals for which transfusion day records and SMR01/cancer/death records were available but excluded from dataset because not study area				
Victoria Hospital (Kirkcaldy)	36,784	321	N	N
Queen Margaret Hospital	26,873	101	N	N
Borders General Hospital	20,188	7	N	N
Gilbert Bain Hospital	3,372	5	N	N
Balfour Hospital, Kirkwall	2,308	5	N	N
Western Isles Hospital	4,665	2	N	N
Cameron Hospital	96	2	N	N
Hospitals not included in study dataset because no year 2000 SMR01/cancer/death records were available				
Simpson Memorial Maternity Pavilion	0	83	N	N
Park House Psychiatric Day Hospital	0	54	N	N
Glenview Unit, Inverness	0	30	N	N
Ashludie Day Hospital	0	13	N	N
Kings Cross Hospital, Dundee	0	9	N	N
Pluscarden Clinic, Dr Gray's Hospital	0	8	N	N
City Hospital, Aberdeen	0	8	N	N
Crieff Cottage Hospital	0	4	N	N
Aberdeen Royal Infirmary	0	3	N	N
Dudhope House, Dundee	0	1	N	N
Dundee Royal Infirmary	0	1	N	N
Royal Edinburgh Hospital	0	1	N	N
Park House Psychiatric Day Hospital	0	1	N	N
Edenhall Hospital, Musselburgh	0	1	N	N
Eastern General Hospital	0	1	N	N
Ladysbridge Hospital	0	1	N	N
St Vincent's Hospital	0	1	N	N

Hospital	Number of SMR01-CD records	Number of TDRs	Study dataset	Denominator data
Hospitals not included in study dataset because no year 2000 SMR01/cancer/death records were available (continued)				
RHSC (Drumchapel)	0	1	N	N
Hospital Cancer Registrations	0	1	N	N
unknown	0	17	N	N
Hospitals outwith study area for which no transfusion day records were available				
Western Infirmary/Gartnavel General	78,389	0	N	N
Glasgow Royal Infirmary	56,359	0	N	N
Monklands Hospital	42,124	0	N	N
Crosshouse Hospital	40,430	0	N	N
Southern General Hospital	39,577	0	N	N
Victoria Infirmary (Glasgow)	38,502	0	N	N
Stobhill Hospital	38,024	0	N	N
The Ayr Hospital	37,795	0	N	N
Royal Alexandra Hospital	36,539	0	N	N
Law Hospital	34,476	0	N	N
Dumfries & Galloway Royal Infirmary	29,368	0	N	N
Stirling Royal Infirmary	28,235	0	N	N
Falkirk and District Royal Infirmary	24,617	0	N	N
Hairmyres Hospital	24,610	0	N	N
Inverclyde Royal Hospital	21,105	0	N	N
RHSC (Yorkhill)	20,205	0	N	N
Vale of Leven District General Hospital	13,476	0	N	N
Canniesburn Hospital	9,701	0	N	N
Stonehouse Hospital	7,002	0	N	N
Lorn & Islands DG Hospital	4,697	0	N	N
Glasgow Dental Hospital and School	3,788	0	N	N
Garrick Hospital	3,339	0	N	N
Forth Park Hospital, Kirkcaldy	2,633	0	N	N
Edinburgh Dental Hospital	2,534	0	N	N
Ayrshire Central and Maternity Hospital	1,843	0	N	N
Dunoon & District General Hospital	1,774	0	N	N
Victoria Infirmary Geriatric Unit (Glasgow)	1,394	0	N	N
Campbeltown Hospital	1,271	0	N	N
St Andrews Memorial Hospital	1,018	0	N	N
Lightburn Hospital	1,009	0	N	N
Biggart Hospital	956	0	N	N
Daliburgh Hospital	721	0	N	N
Isle of Arran War Memorial Hospital	707	0	N	N
Victoria Hospital, Rothesay	613	0	N	N
Davidson Cottage Hospital	580	0	N	N
Mid Argyll Hospital	550	0	N	N
Ravenscraig Hospital	411	0	N	N
Kelso Hospital	378	0	N	N
Park House Psychiatric Day Hospital	369	0	N	N
Crieff Community Hospital	361	0	N	N
Hawick Cottage Hospital	345	0	N	N

Hospital	Number of SMR01-CD records	Number of TDRs	Study dataset	Denominator data
Hospitals outwith study area for which no transfusion day records were available (continued)				
Forfar Infirmary	325	0	N	N
Hay Lodge Hospital	316	0	N	N
Brechin Infirmary	304	0	N	N
Kincardine Community Hospital	304	0	N	N
Bellefield Hospital	299	0	N	N
Cowglen Hospital	289	0	N	N
Islay Hospital	289	0	N	N
Lockhart Hospital	279	0	N	N
Leanchoil Hospital	274	0	N	N
Blairgowrie Cottage Hospital	268	0	N	N
Moffat Hospital	253	0	N	N
Lady Margaret Hospital	242	0	N	N
Kello Hospital	232	0	N	N
Ballochmyle Hospital	229	0	N	N
Kirkcudbright Hospital	222	0	N	N
Aboyne Hospital	217	0	N	N
Coathill Hospital	213	0	N	N
Mental Health Day Service, Stevenston	207	0	N	N
Whytemans Brae Hospital, Kirkcaldy	201	0	N	N
St Margaret's Hospital	197	0	N	N
Knoll Hospital	188	0	N	N
Irvine Memorial Hospital	187	0	N	N
Coldstream Cottage Hospital	159	0	N	N
Lady Home Hospital	153	0	N	N
Newton Stewart Hospital	152	0	N	N
Victoria Cottage Hospital, Kilsyth	149	0	N	N
Castle Douglas Hospital	145	0	N	N
Belhaven Hospital, Dunbar	145	0	N	N
Adamson Hospital	143	0	N	N
Glen O'dee Hospital	142	0	N	N
Udston Hospital, Hamilton	142	0	N	N
Glenrothes Hospital	141	0	N	N
Fleming Cottage Hospital	139	0	N	N
Maidencraig House	137	0	N	N
Pluscarden Clinic, Dr Gray's Hospital	136	0	N	N
Migdale Hospital	130	0	N	N
Aberfeldy Cottage Hospital	128	0	N	N
Witchburn Hospital	128	0	N	N
Randolph Wemyss Memorial Hospital	127	0	N	N
St Brendan's Hospital	123	0	N	N
Victoria Infirmary (Helensburgh)	118	0	N	N
Kincardine O Neil War Memorial Hospital	110	0	N	N
Montrose Royal Infirmary	95	0	N	N
Sister Margaret Cottage Hospital	94	0	N	N
Loanhead Hospital	77	0	N	N
Beatson Oncology Centre	73	0	N	N
Maud Hospital	69	0	N	N

Hospital	Number of SMR01-CD records	Number of TDRs	Study dataset	Denominator data
Hospitals outwith study area for which no transfusion day records were available (continued)				
Lochmaddy Hospital	67	0	N	N
Gesto Hospital, Isle of Skye	62	0	N	N
Netherlea Hospital	52	0	N	N
Dumbarton Joint Hospital	49	0	N	N
Victoria Hospital Annexe	39	0	N	N
Knowepark Hospital	39	0	N	N
Ross House, Inverness	37	0	N	N
Campbell Hospital	31	0	N	N
Sanderson Hospital	31	0	N	N
Mental Health Day Service, Stevenston	31	0	N	N
Merchiston Hospital	28	0	N	N
Shawmill Day Hospital	23	0	N	N
Eastbank Hospital, Kirkwall	18	0	N	N
Strathlea	11	0	N	N
Glenrothes Hospital	10	0	N	N
Wester Moffat Hospital	6	0	N	N
Hyperbaric Centre (Aberdeen)	2	0	N	N
Thornhill Hospital	1	0	N	N
Bellshill Hospital	1	0	N	N

APPENDIX 2.

Table A.2 SPSS programming syntax for study dataset creation and analyses

Development step	Notes
Sort Transfusion day record file (all linked records)	
a. Calculate blood component units used	
COMPUTE *Redused = red_iss - red_rtn*	Repeat for plt, ffp, cry
SELECT IF *Redused>0*	Repeat for plt, ffp, cry
b. Calculate age bands	
COMPUTE *Agebands* *IF (age < 10) ageband = 0* *IF (age >= 10 and age <20) ageband = 1*	Repeat for age bands 2-10 (age=100+)
Sort SMR01/cancer/death file (all linked records)	
a. Recode procedure and diagnosis variables	
STRING OP1 (A8) *COMPUTE OP1 = SUBSTR (op1a, 1, 3)*	Repeat for OP2, 3, 4
STRING diag13 (A8). *COMPUTE diag13 = SUBSTR (diag1, 1, 3)*	Repeat for diag2, 3, 4, 5, 6
b. Define blood using procedure, supplementary procedure, and blood using diagnostic groups	
i. Blood using procedures	
IF (op1="A01" OR op1="A02" OR op1="A03" OR op1="A04" OR op1="A05" OR op1="A06" OR op1="A07" OR op1="A08" OR op1="A09" OR op1="A10") bldprc1 = 1	Repeat for OP2, 3, 4
IF (op1="A12" OR op1="A13" OR op1="A14" OR op1="A15" OR op1="A16" OR op1="A17" OR op1="A18" OR op1="A19" OR op1="A20" OR op1="A21" OR op1="A22") bldprc1 = 2	
IF (op1="A44" OR op1="A45" OR op1="A46" OR op1="A47" OR op1="A48" OR op1="A49" OR op1="A50" OR op1="A51" OR op1="A52" OR op1="A53" OR op1="A54" OR op1="A55" OR op1="A56" OR op1="A57") bldprc1 = 3	
IF (op1="B08" OR op1="B09" OR op1="B10" OR op1="B11" OR op1="B12" OR op1="B13" OR op1="B14" OR op1="B15" OR op1="B16") bldprc1 = 4	

```
IF (op1="B27" OR op1="B28" OR op1="B29" OR op1="B30" OR
op1="B31" OR op1="B32" OR op1="B33" OR op1="B34" OR op1="B35"
OR op1="B36" OR op1="B37") bldprc1 = 5

IF (op1="E19" OR op1="E20" OR op1="E21" OR op1="E22" OR
op1="E23" OR op1="E24" OR op1="E25" OR op1="E26" OR op1="E27")
bldprc1 = 6

IF (op1="E29" OR op1="E30" OR op1="E31" OR op1="E32" OR
op1="E33" OR op1="E34" OR op1="E35" OR op1="E36" OR op1="E37"
OR op1="E38") bldprc1 = 7

IF (op1="E41") bldprc1 = 8

IF (op1="E42") bldprc1 = 9

IF (op1="E14" OR op1="E15" or op1="E16" or op1="E17") bldprc1 = 10

IF (op1="E52") bldprc1 = 11

IF (op1="E53") bldprc1 = 12

IF (op1="E54") bldprc1 = 13

IF (op1="E55") bldprc1 = 14

IF (op1="E57") bldprc1 = 15

IF (op1="E59") bldprc1 = 16

IF (op1="E61") bldprc1 = 17

IF (op1="F34" or op1="F35" or op1="F36" or op1="F37" or op1="F38" or
op1="F39" or op1="F40") bldprc1 = 18

IF (op1="G01" OR op1="G02" OR op1="G03" OR op1="G04" OR
op1="G05" OR op1="G06" OR op1="G07" OR op1="G08" OR op1="G09"
OR op1="G10" OR op1="G11" OR op1="G12" OR op1="G13" ) bldprc1 =
19

IF (op1="G21" OR op1="G22" OR op1="G23" OR op1="G24" OR
op1="G25") bldprc1 = 20

IF (op1="G27" OR op1="G28" OR op1="G29" OR op1="G30" OR
op1="G31" OR op1="G32" OR op1="G33" OR op1="G34" OR op1="G35"
OR op1="G36" OR op1="G37" OR op1="G38" OR op1="G39" OR
op1="G40" OR op1="G41" ) bldprc1 = 21

IF (op1="G49" OR op1="G50" OR op1="G51" OR op1="G52" OR
op1="G53" OR op1="G54" OR op1="G55" OR op1="G56" OR
op1="G57") bldprc1 = 22

IF (op1="G58" OR op1="G59" OR op1="G60" OR op1="G61" OR
op1="G62" OR op1="G63" OR op1="G64" OR op1="G65" OR op1="G66"
OR op1="G67") bldprc1 = 23

IF (op1="G69" OR op1="G70" OR op1="G71" OR op1="G72" OR
op1="G73" OR op1="G74" OR op1="G75" OR op1="G76" OR op1="G77"
OR op1="G78" OR op1="G79" OR op1="G80" OR op1="G81" OR
op1="G82") bldprc1 = 24
```

```
IF (op1="H04" OR op1="H05" OR op1="H06" OR op1="H07" OR
op1="H08" OR op1="H09" OR op1="H10" OR op1="H11") bldprc1 = 25

IF (op1="H33") bldprc1 = 26

IF (op1="J01") bldprc1 = 27

IF (op1="J02") bldprc1 = 28

IF (op1="J03" OR op1="J04" OR op1="J05" OR op1="J06"
OR op1="J07" OR op1="J08" OR op1="J09" OR op1="J10" OR
op1="J11" OR op1="J12" OR op1="J13" OR op1="J14" OR op1="J15"
OR op1="J16") bldprc1 = 29

IF (op1="J18" OR op1="J19" OR op1="J20" OR op1="J21"
OR op1="J22" OR op1="J23") bldprc1 = 30

IF (op1="J27" OR op1="J28" OR op1="J29" OR op1="J30"
OR op1="J31" OR op1="J32" OR op1="J33" OR op1="J34" OR
op1="J35" OR op1="J36" OR op1="J37") bldprc1 = 31

IF (op1="J54" OR op1="J55" OR op1="J56" OR op1="J57"
OR op1="J58" OR op1="J59" OR op1="J60" OR op1="J61" OR
op1="J62" OR op1="J63" OR op1="J64" OR op1="J65") bldprc1 = 32

IF (op1="J69" OR op1="J70") bldprc1 = 33

IF (op1="K01" OR op1="K02") bldprc1 = 34

IF (op1="K25" OR op1="K26" OR op1="K27" OR op1="K28" OR
op1="K29" OR op1="K30" OR op1="K31" OR op1="K32" OR op1="K33"
OR op1="K34" OR op1="K35" OR op1="K36" OR op1="K37" OR
op1="K38") bldprc1 = 35

IF (op1="K40" OR op1="K41" OR op1="K42" OR op1="K43" OR
op1="K44" OR op1="K45" OR op1="K46" OR op1="K47" OR op1="K48")
AND (op1a ne"K442" OR op1a ne"K456" OR
op1a ne"K465") bldprc1 = 36

IF (op1a="K442" OR op1a="K456" OR op1a="K465")
bldprc1 = 37

IF (op1="L01" OR op1="L02" OR op1="L03" OR op1="L04"
OR op1="L05" OR op1="L06" OR op1="L07" OR op1="L08" OR
op1="L09" OR op1="L10" OR op1="L11" OR op1="L12") bldprc1 = 38

IF (op1="L13") bldprc1 = 39

IF (op1="L18" OR op1="L20") bldprc1 = 40

IF (op1="L16" OR op1="L19" OR op1="L21" OR op1="L22"
OR op1="L23" OR op1="L24" OR op1="L25") bldprc1 = 41

IF (op1="L26") bldprc1 = 42

IF (op1="L29" OR op1="L30" OR op1="L31" OR op1="L32"
OR op1="L33" OR op1="L34" OR op1="L35" OR op1="L36" OR
op1="L37" OR op1="L38" OR op1="L39") bldprc1 = 43

IF (op1="L41" OR op1="L42" OR op1="L43") bldprc1 = 44

IF (op1="L45" OR op1="L46") bldprc1 = 45
```

IF (op1="L77") bldprc1 = 46

IF (op1="L91") bldprc1 = 47

IF (op1="M01") bldprc1 = 48

IF (op1="M02" OR op1="M03" OR op1="M04" OR op1="M05" OR op1="M06" OR op1="M07" OR op1="M08") bldprc1 = 49

IF (op1a="M34" OR op1="M35") bldprc1 = 50

IF (op1="M36" OR op1="M37" OR op1="M38" OR op1="M39" OR op1="M40" OR op1="M41") bldprc1 = 51

IF (op1="M51" OR op1="M52" OR op1="M53" OR op1="M54" OR op1="M55" OR op1="M56" OR op1="M57" OR op1="M58") bldprc1 = 52

IF (op1="M61" OR op1="M62" OR op1="M63" OR op1="M64") bldprc1 = 53

IF (op1="Q07" OR op1="Q08") bldprc1 = 54

IF (op1="T85") bldprc1 = 55

IF (op1="V14") bldprc1 = 56

IF (op1="W10" OR op1="W11" OR op1="W12" OR op1="W13" OR op1="W14" OR op1="W15" OR op1="W16" OR op1="W17" OR op1="W18" OR op1="W19" OR op1="W20" OR op1="W21" OR op1="W22" OR op1="W23") bldprc1 = 57

IF (op1="W24" OR op1="W25" OR op1="W26") bldprc1 = 58

IF (op1="W36") bldprc1 = 59

IF (op1="W37" OR op1="W38" OR op1="W39") AND (op1a ne"W373" OR op1a ne"W383" OR op1a ne"W393") bldprc1 = 60

IF (op1a="W373" OR op1a="W383" OR op1a="W393") bldprc1 = 61

IF (op1="W40" OR op1="W41" OR op1="W42") AND (op1a ne"W403" OR op1a ne"W413" OR op1a ne"W423") bldprc1 = 62

IF (op1a="W403" OR op1a="W413" OR op1a="W423") bldprc1 = 63

IF (op1="W46" OR op1="W47") bldprc1 = 64

ii. Supplementary procedures

IF (op1="E49") supp1 = 1

Repeat for OP2, 3, 4

IF (op1="G14" OR op1="G15" OR op1="G16" OR op1="G17" OR op1="G18" OR op1="G19") supp1 = 2

IF (op1="G43" OR op1="G44" OR op1="G45") supp1 = 3

IF (op1="H20" OR op1="H21" OR op1="H22" OR op1="H23" OR op1="H24" OR op1="H25" OR op1="H26" OR op1="H27" OR op1="H28") supp1 = 4

IF (op1="M09" OR op1="M10" OR op1="M11" OR op1="M12") supp1 = 5

IF (op1="M42" OR op1="M43" OR op1="M44" OR op1="M45") supp1 = 6

IF (op1="M65" OR op1="M66" OR op1="M67") supp1 = 7

IF (op1="X32" OR op1="X33") supp1 = 8

IF (op1="X35" OR op1="X37" OR op1="X38") supp1 = 9

IF (op1="X40" OR op1="X41" OR op1="X42") supp1 = 10

IF (op1="X55") supp1 = 11

iii. Blood using diagnoses

IF (diag13="C81" or diag13="C82" or diag13="C83" or diag13="C84" or diag13="C85") bldiag1 = 22
IF (diag13="C90") bldiag1 = 23
IF (diag13="C91" or diag13="C92" or diag13="C93" or diag13="C94" or diag13="C95") bldiag1 = 24
IF (diag13="C96") bldiag1 = 25
IF (diag13="D45" or diag13="D46") bldiag1 = 26

Repeat for C51-21, C32-34, C53, C54, C56, C61, C62, C70, C71, [D50-D53], [D55-D59], [D60-D64], [D65-D69], [D70-D77], [D80-D89], I85, [K25-K30], K44, K31, K50, K70, K71, K74, K920, K922, N17, N18

iv. Value labels for case groups

VALUE LABELS *bldprc1 bldprc2 bldprc3 bldprc4 bldproc*
1 'Brain'
2 'Ventricle'
3 'Spinal cord and contents of spinal canal'
4 'Thyroid or parathyroid'
5 'Breast'
6 'Pharynx'
7 'Larynx'
8 'Open placement of prosthesis in trachea'
9 'Exteriorisation of trachea'
10 'Sinus'
11 'Other operations on bronchus'
12 'Transplant of lung'
13 'Excision of lung'
14 'Open extirpation of lesion of lung'
15 'Other open ops on lung'
16 'Other ops on lung'
17 'Open ops on mediastinum'
18 'Tonsil and mouth'
19 'Open ops on oesophagus'
20 'Other ops on oesoph'
21 'Open ops on stomach and pylorus'
22 'Duodenum'
23 'Jejunum'
24 'Ileum'
25 'Excision of colon'
26 'Excision of rectum'
27 'Transplant of liver'
28 'Partial excision of liver'
29 'Other ops on liver'
30 'Gall bladder'
31 'Open ops on bile duct'
32 'Open ops on pancreas'
33 'Excision of spleen'

Underlined case groups used in study

34 'Heart transplant'
35 'Valves and adjacent structures'
36 'Open bypass graft operations (minus revisions)'
37 'Open bypass graft operations revisions'
38 'Open operations on GV and PA'
39 'Transluminal ops on PA'
40 'Emergency replace aneurysm aorta'
41 'Other ops on aorta'
42 'Transluminal ops on aorta'
43 'Carotid cerebral and subclavian'
44 'Reconstruction of renal artery'
45 'Open ops on visceral branches of aorta'
46 'Connection vena cava or branch of VC'
47 'Other vein related operations'
48 'Transplantation of kidney'
49 'Other open ops on kidney'
50 'Excision of bladder'
51 'Other open ops on bladder'
52 'Ops on female bladder'
53 'Open ops on prostate'
54 'Hysterectomy'
55 'Block dissection of lymph nodes'
56 'Excision of mandible'
57 'Open reduction fracture'
58 'Closed reduction fracture'
59 'Diagnostic puncture of bone'
60 'Total hip replacement (minus revisions)'
61 'Total hip replacement revisions'
62 'Total knee replacement (minus revisions)'
63 'Total knee replacement revisions'
64 'Replace head of femur'

VALUE LABELS supp1 supp2 supp3 supp4
1 'Endoscopy of lower respiratory tract'
2 'Endoscopic ops on oesoph'
3 'Endoscopy of upper GI tract'
4 'Endoscopic ops on colon'
5 'Endoscopic ops on kidney'
6 'Endoscopic ops on bladder'
7 'Endoscopic ops on prostate'
8 'Blood transfusion'
9 'Chemotherapy'
10 'Compensation for renal failure'
11 'Other ops on unspecified organ'

VALUE LABELS bldiag1 bldiag2 bldiag3 bldiag4 bldiag5 bldiag6
1 'Mal neo of Oesophagus'
2 'Mal neo of Stomach'
3 'Mal neo of Small Intestine'
4 'Mal neo of Colon'
5 'Mal neo of Rectosigmoid'
6 'Mal neo of Rectum'
7 'Mal neo of Anal Canal'
8 'Mal neo of Larynx'
9 'Mal neo of Other Biliary'
10 'Mal neo of Pancreas'
11 'Mal neo of Other Digestive'
12 'Mal neo of Gallbladder'
13 'Mal neo of Trachea'
14 'Mal neo of Bronchus'
15 'Mal neo of Cervix'
16 'Mal neo of Uterus'

17 'Mal neo of Ovary'
18 'Mal neo of Prostate'
19 'Mal neo of Testis'
20 'Mal neo of Meninges'
21 'Mal neo of Brain'
22 'Lymphoma'
23 'Myeloma'
24 'Leukaemia'
25 'Other & Unspec haematopoietic & related tissues'
26 'Polycythaemia & myelodysplastic syndromes'
27 'Oesophageal varices'
28 'Crohn's Disease'
29 'Ulcerative Colitis'
30 'Haematemesis'
31 'Melaena'
32 'Gastrointestinal haemorrhage Unspec'
33 'Acute renal failure'
34 'Chronic renal failure'
35 'Peptic ulcer'
36 'Alcoholic liver disease'
37 'Toxic liver disease'
38 'Fibrosis/Cirrhosis of liver'
39 'Diaphragmatic hernia'
40 'Other diseases of stomach & duodenum'
41 'Nutritional anaemias'
42 'Haemolytic anaemias'
43 'Aplastic and other anaemias'
44 'Coagulation defects, purpura and other haemorrhagic conditions'
45 'Other diseases of blood and blood forming organs'
46 'Certain disorders involving the immune mechanism'

Underlined case groups used in study

RECODE (SYSMIS=0)

Define Group A procedures

IF (bldprc4=1 or bldprc4=4 or bldprc4=8 or bldprc4=13 or bldprc4=14 or bldprc4=16 or bldprc4=19 or bldprc4=25 or bldprc4=26 or bldprc4=27 or bldprc4=28 or bldprc4=34 or bldprc4=35 or bldprc4=36 or bldprc4=37 or bldprc4=40 or bldprc4=41 or bldprc4=44 or bldprc4=48 or bldprc4=49 or bldprc4=53 or bldprc4=54 or bldprc4=57 or bldprc4=58 or bldprc4=60 or bldprc4=61 or bldprc4=62 or bldprc4=63 or bldprc4=64) bldproc = bldprc4

Repeat for bldprc3, 2, 1 [NB. Reverse order]

Define Group B diagnoses

IF (bldiag1=22 or bldiag1=23 or bldiag1=24 or bldiag1=26) haemdiag1= bldiag1
RECODE haemdiag1 (SYSMIS=0)

IF (bldiag2=22 or bldiag2=23 or bldiag2=24 or bldiag2=26) and (haemdiag1=0) haemdiag1= bldiag2

IF (bldiag3=22 or bldiag3=23 or bldiag3=24 or bldiag3=26) and (haemdiag1=0) haemdiag1= bldiag3

IF (bldiag4=22 or bldiag4=23 or bldiag4=24 or bldiag4=26) and (haemdiag1=0) haemdiag1 = bldiag4

IF (bldiag5=22 or bldiag5 =23 or bldiag5=24 or bldiag5=26) and (haemdiag1=0) haemdiag1 = bldiag5

IF (bldiag6=22 or bldiag6=23 or bldiag6=24 or bldiag6=26) and (haemdiag1=0) haemdiag1 = bldiag6

VALUE LABELS maindiag
1 'Lymphoma'
2 'Myeloma'
3 'Leukaemia'
4 'Other'
5 'MDS'

Restructure SMR01/cancer/death records into single records

CASESTOVARS
/ID = isd_no
/GROUPBY = INDEX
/COUNT = episode.

Merge Transfusion day records and restructured SMR01/cancer/death records

GET Transfusion day records file

MATCH FILES by ISD_NO to SMR01/cancer/death records

SAVE AS Study database

Date attribution

IF (doa.1 - evt_dte <= 604800 & evt_dte - dod.1 <= 0) da1 = 1

Repeat for all SMR01/cancer/death records i.e. to da123

RECODE (SYSMIS=0)

COMPUTE tlda = SUM (da1, 2, 3 ... 123)

Group A. Surgical patients: number of red blood cell units used (rctp) and red cell using procedure (rcup)

IF (da1=1 and (bldproc.1>0)) rctp1 = redused

Repeat for all SMR01/cancer/death records i.e. to bldproc.123

IF (da1=1 and (bldproc.1>0)) rcup1 = bldproc.1

RECODE (SYSMIS=0)

COMPUTE tlrctp = SUM (rctp1, 2, 3 ... 123)

Number of red cell using procedures (nrcup)

COMPUTE nrcup = tlrctp / redused

Main red cell using procedure (procedure)

Repeat for all SMR01/cancer/death records i.e. to rcup123

IF (rcup1>0) procedure = rcup1

RECODE procedure (SYSMIS=0)

IF (procedure=0 and rcup2>0) procedure = rcup2

Group B. Haematological patients: diagnosis (haemdiag)

AGGREGATE SMR01/caner/death records by ISD_NO and return 1ST maindiag (rename "HAEMDIAG").

MATCH back to Merged STEP Database

APPENDIX 3.

Table A.3 Excerpt from STED regional Surgical Blood Use report (2002/3-2005/6)

OPCS Chapter	Blood Using Procedures (3 Character OPCS codes)	2002/03				2003/04				2004/05				2005/06			
		No of Episodes	% Episodes Transfused	RBC Units	RBC/Episode	No of Episodes	% Episodes Transfused	RBC Units	RBC/Episode	No of Episodes	% Episodes Transfused	RBC Units	RBC/Episode	No of Episodes	% Episodes Transfused	RBC Units	RBC/Episode
K. Heart	Coronary Replacement Operations (Inclusive Equivalent)	604	44.9 %	741	1.3	541	51.8 %	997	1.8	432	48.8 %	718	1.6	432	48.6 %	842	1.5
	Revision Coronary Replacement Operations	4	100.0 %	20	5.0	9	66.6 %	21	2.3	10	60.0 %	24	2.4	8	37.5 %	15	2.0
	Valves & Adjacent Structures	81	67.9 %	274	3.8	105	71.3 %	322	3.0	95	64.6 %	269	2.8	121	53.7 %	274	2.3
OPCS Chapter Total		858	48.3 %	1,035	1.8	826	56.8 %	1,340	2.8	558	51.8 %	1,011	1.8	561	49.6 %	995	1.7
L. Arteries and Veins	Emer. Replacement of Aneurysmal Aorta	19	89.5 %	202	10.6	34	82.3 %	276	11.0	32	84.4 %	282	8.8	16	68.0 %	114	10.4
	Open Ops on Great Vessels & Pulmonary Artery	9	0.0%	8	0.9	9	0.0%	8	0.9	2	100.0 %	9	4.5	8	0.0%	0	0.0
	Open Ops on Visceral Branches of Aorta	6	0.0%	8	0.0	1	0.0%	0	0.0	1	100.0 %	2	2.0	2	50.0 %	4	2.0
	Other Non Emer Operations on Aorta	45	49.9 %	145	3.2	52	53.8 %	158	3.0	38	44.7 %	65	1.5	44	29.5 %	96	2.2
	Reconstruction of Renal Artery	21	9.6 %	7	0.3	24	2.7 %	6	0.3	29	13.8 %	36	1.2	31	19.4 %	28	0.9
OPCS Chapter Total		85	49.2 %	354	4.2	103	48.5 %	442	4.3	102	56.8 %	389	3.8	87	32.3 %	242	2.8
M. Urinary	Endoscopic Ops on Prostate & Outlet of Male Bladder	248	6.0 %	61	0.3	271	6.6 %	72	0.3	248	4.0 %	30	0.2	204	3.2 %	60	0.1
	Excision of Bladder	20	70.0 %	92	4.6	24	45.8 %	52	2.2	21	42.9 %	38	1.9	16	56.3 %	30	1.9
	Open Ops on Prostate & Outlet of Male Bladder	22	54.5 %	40	1.8	32	40.6 %	87	2.7	34	55.9 %	93	2.7	26	28.6 %	36	1.3
	Operations on Female Bladder	143	2.5 %	10	0.1	172	0.6 %	2	0.0	173	0.6 %	2	0.0	229	0.8 %	2	0.0
	Other Open Operations on Bladder	10	15.8 %	6	0.3	30	13.3 %	12	0.4	25	12.0 %	10	0.4	14	21.4 %	8	0.6
	Other Open Operations on Kidney	104	20.8 %	120	1.2	104	22.1 %	82	0.9	84	27.4 %	109	1.3	86	23.5 %	86	1.0
OPCS Chapter Total		596	13.3 %	359	0.6	633	10.7 %	317	0.5	585	11.1 %	286	0.5	659	7.9 %	208	0.3
Q. Ob/gyn Female Genital Tract	Hysterectomy	462	6.3 %	92	0.2	439	9.1 %	172	0.4	482	6.4 %	111	0.2	486	7.8 %	116	0.2
OPCS Chapter Total		462	6.3 %	92	0.2	439	9.1 %	172	0.4	482	6.4 %	111	0.2	486	7.8 %	116	0.2
T. Soft Tissue	Block Dissection Of Lymph Nodes	84	13.1 %	34	0.4	71	9.9 %	18	0.3	90	8.9 %	22	0.2	95	2.1 %	7	0.1
OPCS Chapter Total		84	13.1 %	34	0.4	71	9.9 %	18	0.3	90	8.9 %	22	0.2	95	2.1 %	7	0.1
V. Bones & Joints of Skull & Spine	Excision Of Mandible	6	0.0%	0	0.0	4	0.0%	0	0.0	7	14.3 %	2	0.3	5	0.0%	0	0.0
OPCS Chapter Total		6	0.0%	0	0.0	4	0.0%	0	0.0	7	14.3 %	2	0.3	5	0.0%	0	0.0
W. Other Bones & Joints	Closed Reduction of Fracture	951	11.8 %	311	0.3	990	12.9 %	413	0.4	844	11.3 %	239	0.3	863	10.1 %	248	0.3
	Open Reduction of Fracture	845	13.6 %	558	0.7	881	9.8 %	372	0.4	948	10.4 %	428	0.5	829	8.4 %	371	0.4
	Primary Total Hip Replacement (formal revisions)	548	31.8 %	494	0.9	582	24.6 %	359	0.6	386	20.3 %	299	0.9	730	16.8 %	299	0.4
	Primary Total Knee Replacement (formal revisions)	396	17.6 %	159	0.4	436	11.2 %	115	0.3	367	8.2 %	69	0.2	481	6.7 %	73	0.2
	Replacement of Head of Femur	245	23.7 %	133	0.5	252	23.3 %	166	0.7	286	21.6 %	157	0.6	306	18.0 %	127	0.4
	Revision Total Hip Replacement	96	68.4 %	257	2.6	107	71.0 %	301	2.8	105	48.5 %	179	1.7	119	46.3 %	158	1.3
	Revision Total Knee Replacement	31	32.3 %	23	0.7	24	37.5 %	46	2.0	39	33.3 %	27	0.7	50	20.0 %	16	0.3
OPCS Chapter Total		3,168	18.4 %	1,935	0.6	3,293	16.9 %	1,770	0.5	3,167	14.7 %	1,392	0.4	3,478	12.7 %	1,292	0.4
All Procedures		9,395	15.2 %	6,834	0.8	8,580	15.8 %	5,519	0.6	9,306	12.4 %	4,765	0.5	9,892	11.6 %	4,416	0.4

Stewart, Blood Use Data Project Manager, Better Blood Transfusion Programme

REFERENCES

Anderson,SA., Menis,M., O'Connell,K., & Burwen,DR. (2007) Blood use by inpatient elderly population in the United States. *Transfusion*, **47**, 582-592.

Aul,C., Germing,U., Gattermann,N., & Minning,H. (1998) Increasing incidence of myelodysplastic syndromes: Real or fictitious? *Leukemia Research*, **22**, 93-100.

Baele,Ph., Beguin,C., Waterloos,E., Dupont,E., Lambermont,M., Vandermeersch,E., Dicker,D., & Peresino,A. (1998) The Belgium BIOMED Study about transfusion for surgery. *Acta anaesthesiologica Belgica*, **49**, 243-303.

Bell,K., Stott,K., Sinclair,CJ., Walker,WS., & Gillon,J. (1992) A controlled trial of intra-operative autologous transfusion in cardiothoracic surgery measuring effect on transfusion requirements and clinical outcome. *Transfusion Medicine*, **2**, 295-300.

Bierbaum,BE., Callaghan,JJ., Galante,JO., Rubash,HE., Tooms,RE., & Welch,RB. (1999) An Analysis of Blood Management in Patients Having a Total Hip or Knee Arthroplasty. *Journal of Bone and Joint Surgery*, **81**, 2-10.

Blajchman,MA. (2005) Landmark studies that have changed the practice of transfusion medicine. *Transfusion*, **45**, 1523-1530.

Boralessa,H., Boralessa,H., Contreras,M., Lang-Stevenson,A., Knowles,S., & Cockburn,H. (2000) Retrospective Study on Red Cell Usage in Primary Total Knee Replacement Surgery. *Vox Sanguinis*, **79**, 231-234.

Boralessa,H., Boralessa,H., Contreras,M., Lang-Stevenson,A., & DeSilva,A. (2001) Effectiveness of a protocol to improve transfusion practice in knee replacement surgery. *Vox Sanguinis*, **81**, 248-253.

Bray,TJ., Salil,P., Weiss,HA., & Porter,J. (2003) Transfusion medicine in India: a survey of current practice. *Transfusion Medicine*, **13**, 17-24.

Brecher,ME. & Hay,SN. (2005) Bacterial Contamination of Blood Components. *Clinical Microbiology Reviews*, **18**, 195-204.

Brunskill,SJ., Tusold,A., Benjamin,S., Stanworth,SJ., & Murphy,MF. (2007) A systematic review of randomized controlled trials for plasma exchange in the treatment of thrombotic thrombocytopenic purpura. *Transfusion Medicine*, **17**, 17-35.

Burnouf,T. & Padilla,A. (2006) Current strategies to prevent transmission of prions by human plasma derivatives. *Transfusion Clinique et Biologique*, **13**, 320-328.

Burns,A. & Bourne,RB. (2006) Economics of revision total hip arthroplasty. *Current Orthopaedics*, **20**, 203-207.

Canadian Institute for Health Information (CIHI). (2004) Acute Care Grouping Methodologies: From diagnosis-related groups to case mix groups development. Ottawa, Canadian Institute for Health Information.

Cancer Research UK (online) Cancer Statistics. *http://.info.cancerresearchuk.org/cancerstats,* Cancer Research UK.

Carless,PA., Henry,DA., Moxey,AJ., O'Connell,DL., Brown,T., & Fergusson,DA. (2006) Cell salvage for minimising peri-operative allogeneic blood transfusion. *Cochrane Database of Systematic Reviews,* Art. No.: CD001888. DOI: 10.1002/14651858.CD001888.pub2.

Carson,JL., Hill,SR., Carless,PA., Hebert,PC., & Henry,DA. (2002) Transfusion triggers: a systematic review of the literature. *Transfusion Medicine Reviews,* **16,** 187-199.

Cartwright,RA., Gilman,EA., & Gurney,KA. (1999) Time trends in incidence of haematological malignancies and related conditions. *British Journal of Haematology,* **106,** 281-295.

Chapman,J. & Hick,R. (2003) Monitoring the nation's blood supply. *Transfusion,* **43,** 1639.

Chaudhary,R., Singh,H., Verma,A., & Ray,V. (2005) Evaluation of fresh frozen plasma usage at a tertiary care hospital in North India. *ANZ Journal of Surgery,* **75,** 573-576.

Chiavetta,JA., Herst,R., Freedman,J., Axcell,TJ., Wall,AJ., & Rooy,SC. (1996) A survey of red cell use in 45 hospitals in central Ontario, Canada. *Transfusion,* **36,** 699-706.

Churchill,WH., McGurk,S., Chapman,RH., Wallace,EL., Bertholf,MF., Goodnough,LT., Kao,KJ., Olson,JD., Woodson,RD., & Surgenor,DM. (1998) The Collaborative Hospital Transfusion Study: variations in use of autologous blood account for hospital differences in red cell use during primary hip and knee surgery. *Transfusion,* **38,** 530-539.

Clark,P. & Mintz,P. (2001) Transfusion triggers for blood components. *Current Opinion in Hematology,* **8,** 387-391.

Cobain,TJ. (2004) Fresh blood product manufacture, issue and use: A chain of diminishing returns? *Transfusion Medicine Reviews,* **18,** 279-292.

Cobain,TJ., Vamvakas,EC., Wells,A., & Titlestad,K. (2007) A survey of the demographics of blood use. *Transfusion Medicine,* **17,** 1-15.

Coni,N. (2002) Medicine and the Spanish Civil War. *Journal of the Royal Society of Medicine,* **95,** 147-150.

Cook,SS. & Epps,J. (1991) Transfusion practice in central Virginia. *Transfusion,* **31,** 355-360.

Coovadia,AS., Pinkerton,PH., & Sharkey,PW. (1992) Utilisation of blood components by a regional trauma unit. *Canadian Society for Transfusion Medicine (CSTM) Bulletin* **4**(3), 34-39.

Corwin,HL., Parsonnet,KC., & Gettinger,A. (1995) RBC transfusion in the ICU. Is there a reason? *Chest*, **108**, 767-771.

Criddle,LM., Eldredge,DH., & Walker,J. (2005) Variables Predicting Trauma Patient Survival Following Massive Transfusion. *Journal of Emergency Nursing*, **31**, 236-242.

Davies,L., Brown,TJ., Haynes,S., Payne,K., Elliott,RA., & McCollum,C. (2006) Cost-effectiveness of cell salvage and alternative methods of minimising peri-operative allogeneic blood transfusion: a systematic review and economic model. *Health Technology Assessment*, **10**(44), 1-229.

Department of Health (DOH). (1998) Better Blood Transfusion. HSC 1998/224. London, Department of Health.

Department of Health (DOH). (2002) Better Blood Transfusion: Appropriate Use of Blood. HSC 2002/009. London, Department of Health.

Dobra, S (personal communication) Department of Health Economics and Operational Research Division, Department of Health, London.

Donaldson, L. (2003) On the state of the public health. Annual Report of the Chief Medical Officer. London, Department of Health.

Dzik,WH., Corwin,H., Goodnough,LT., Higgins,M., Kaplan,H., Murphy,M., Ness,P., Shulman,IA., & Yomtovian,R. (2003) Patient safety and blood transfusion: new solutions. *Transfusion Medicine Reviews*, **17**, 169-180.

Economic and Social Research Council (ESRC). (2004) The demographic trends in Scotland. A shrinking and ageing population. ESRC Seminar Series: Mapping the public policy landscape. Economic and Social Research Council.

Ensolease,ME., Imarengiaye,CO., & Awodu,OA. (2004) Donor blood procurement and utilisation at the University of Benin Teaching Hospital, Benin City. *African Journal of Reproductive Health*, **8**, 59-63.

Farion,KJ., McLellan,BA., & Boulanger,BR. (2007) Changes in Red Cell Transfusion Practice among Adult Trauma Victims. *The Journal of Trauma: Injury, Infection, and Critical Care*, **44**, 583-587.

Farrar,D., Robertson,MS., Hogan,CJ., Roy,S., Boyce,CA., Howe,BD., Presneill,JJ., & Cade,JF. (2004) Blood usage in an Australian intensive care unit: have we met best practice goals? *Anaesthia Intensive Care*, **32**, 775-780.

French,CJ., Bellomo,R., Finfer,SR., Lipman,J., Chapman,M., & Boyce,NW. (2002) Appropriateness of red blood cell transfusion in Australasian intensive care practice. *Medical Journal of Australia* , **177**, 548-551.

Friedman,BA., Burns,TL., & Schork,MA. (1979) A study of blood utilization by diagnosis, month of transfusion, and geographic region of the United States. *Transfusion*, **19**, 511-525.

General Register Office for Scotland (GRO) (online) Population projections and estimates *http://www.gro-scotland.gov.uk/statistics/population.html*

Goodnough,LT., Johnston,MF., Shah,T., & Chernosky,A. (1989) A two-institution study of transfusion practice in 78 consecutive adult elective open-heart procedures. *American Journal of Clinical Pathology*, **91**, 468-472.

Goodnough,LT., Johnston,MF., & Toy,PT. (1991) The variability of transfusion practice in coronary artery bypass surgery. Transfusion Medicine Academic Award Group. *JAMA: The Journal of the American Medical Association*, **265**, 86-90.

Goodnough,LT., Brecher,ME., Kanter,MH., & AuBuchon,JP. (1999) Transfusion Medicine: First of Two Parts (Blood Transfusion). *The New England Journal of Medicine*, **340**, 438-447.
Grey,DE., Smith,V., Villanueva,G., Richards,B., Augustson,B., & Erber,WN. (2006) The utility of an automated electronic system to monitor and audit transfusion practice. *Vox Sanguinis*, **90**, 316-324.

Harley,K. and Jones,C. (1996) Quality of Scottish Morbidity record (SMR) data. *Health Bulletin* **54**, 410-417

Hasley,PB., Lave,JR., Hanusa,BH., Arena,VC., Ramsey,G., Kapoor,WN., & Fine,MJ. (1995) Variation in the use of red blood cell transfusions. A study of four common medical and surgical conditions. *Medical Care*, **33**, 1145-60.

Hebert,PC., Wells,G., Blajchman,MA., Marshall,J., Martin,C., Pagliarello,G., Tweeddale,M., Schweitzer,I., Yetisir,E., & The Transfusion Requirements in Critical Care (TRICC) Investigators for the Canadian Critical Care Trials Group (1999a) A Multicenter, Randomized, Controlled Clinical Trial of Transfusion Requirements in Critical Care. *The New England Journal of Medicine*, **340**, 409-417.

Hebert,PC., Wells,G., Martin,C., Tweeddale,M., Marshall,J., Blajchman,M., Pagliarello,G., Sandham,D., Schweitzer,I., Boisvert,D., Calder,L., & for the Transfusion Requirements in Critical Care (TRICC) Investigators and the Canadian Critical Care Trials Group (1999b) Variation in red cell transfusion practice in the intensive care unit: a multicentre cohort study. *Critical Care*, **3**, 57-63.

Higgins,JPT. & Green,S. (2006) Cochrane Handbook for Systematic Reviews of Interventions 4.2.6. *http://www.cochrane.org/resources/handbook/hbook.htm.* Cochrane Collaboration.

Hill,SR., Carless,PA., Henry,DA., Carson,JL., Hebert,PC., McClelland,DBL., & Henderson,KM. (2002) Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. *Cochrane Database Systematic Reviews*, **2**, CD002042.

Huët,C., Salmi,LR., Fergusson,D., Koopman-van Gemert,A., Rubens,F., & Laupacis,A. (1999) A Meta-Analysis of the Effectiveness of Cell Salvage to Minimize Peri-operative Allogeneic Blood Transfusion in Cardiac and Orthopaedic Surgery. *Anesthesia Analgesia*, **89**, 861.

Hui,C.H., Williams,I., & Davis,K. (2005) Clinical audit of the use of fresh-frozen plasma and platelets in a tertiary teaching hospital and the impact of a new transfusion request form. *Internal Medicine Journal*, **35**, 283-288.

Hutton,B., Fergusson,D., Tinmouth,A., McIntyre,L., Kmetic,A., & Hebert,PC. (2005) Transfusion rates vary significantly amongst Canadian medical centres: [Les taux de transfusion varient de facon significative dans les centres medicaux canadiens]. *Canadian Journal of Anesthesia*, **52**, 581-590.

Information and Statistics Division (ISD). (2004) Data Quality Assurance Report on Acute Inpatient/Day Case Data 2000-2002. ISD, Common Services Agency, NHS Scotland.
James,RM., Brown,S., Parapia,LA., & Williams,AT. (2001) The impact of a 10-year audit cycle on blood usage in a district general hospital. *Transfusion Medicine*, **11**, 371-375.

The vCJD Working Party of the Standing Advisory Committee on Transfusion Transmitted Infections. (2007) Position Statement 01: Creutzfeldt-Jakob Disease. *http://www.transfusionguidelines.org.uk/index.asp?Publication=DL&Section=12&pageid=794.* Joint United Kingdom Blood Transfusion Services (UKBTS) and National Institute for Biological Standards and Control (NIBSC) Professional Advisory Committee (JPAC).

Joshi,GP. & Landers,DF. (1998) Audit in transfusion practice. *Journal of Evaluation in Clinical Practice*, **4**, 141-146.

Kanter,MH. (1998) The Transfusion Audit as a Tool to Improve Transfusion Practice: a Critical Appraisal. *Transfusion Science*, **19**, 69-81.

Karkouti,K., Cohen,MM., McCluskey,SA., & Sher,GD. (2001) A multivariable model for predicting the need for blood transfusion in patients undergoing first-time elective coronary bypass graft surgery. *Transfusion*, **41**, 1193-1203.

Kendrick,S. and Clarke,J. (1993) The Scottish record linkage system. *Health Bulletin* **51**, 72-79.

Kendrick,S. (1997) The development of record linkage in Scotland: The responsive application of probability matching. NHS Scotland.

Kleinman,S., Marshall,D., AuBuchon,J., & Patton,M. (2004) Survival after transfusion as assessed in a large multistate US cohort. *Transfusion*, **44**, 386-390.

Last,JM. (2001) *A Dictionary of Epidemiology*, 4th Edition. New York, Oxford University Press.

Lemos,MJ. & Healy,WL. (1996) Current Concepts Review - Blood Transfusion in Orthopaedic Operations. *Journal of Bone and Joint Surgery*, **78**, 1260-1271.

Leukaemia Research Foundation (online) Disease information and statistics *http://www.lrf.org.uk*

Lim,YA., Lee,WG., Cho,SR., Hyun,BH., & Sc,D. (2004) A study of blood usage by diagnoses in a Korean university hospital. *Vox Sanguinis*, **86**, 54-61.

Lin,C.K. (2004) Practical approaches to limited resources. *Vox Sanguinis*, **87**, 172-175.

Llewelyn,CA., Hewitt,PE., Knight,R., Amar,K., Cousens,S., Mackenzie,J., & Will,RG. (2004) Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. *The Lancet*, **363**, 417-421.

Ma,M., Eckert,K., Ralley,F., & Chin-Yee,I. (2005) A retrospective study evaluating single-unit red blood cell transfusions in reducing allogeneic blood exposure. *Transfusion Medicine*, **15**, 307-312.

Maclennan,S. & Murphy,MF. (2001) Survey of the use of whole blood in current blood transfusion practice. *Clinical and Laboratory Haematology*, **23**, 391-396.

Madjdpour,C. & Spahn,DR. (2005) Allogeneic red blood cell transfusions: efficacy, risks, alternatives and indications. *British Journal of Anaesthesia*, **95**, 33-42.

Malfroy,M., Llewelyn,CA., Johnson,T., & Williamson,LM. (2004) Using patient-identifiable data for epidemiological research. *Transfusion Medicine*, **14**, 275-279.

Mallett,SV., Peachey,TD., Sanehi,O., Hazlehurst,G., & Mehta,A. (2000) Reducing red blood cell transfusion in elective surgical patients: the role of audit and practice guidelines. *Anaesthesia*, **55**, 1013-1019.

Mathoulin-Pelissier,S., Salmi,LR., Verret,C., & Demoures,B. (2000) Blood transfusion in a random sample of hospitals in France. *Transfusion*, **40**, 1140-1146.

Maxwell,EL., Metz,J., Haeusler,MN., & Savoia,HF. (2002) Use of red blood cell transfusions in surgery. *ANZ Journal of Surgery*, **72**, 561-566.

McClelland,DBL. & Contreras,M. (2005a) Appropriateness and safety of blood transfusion. *BMJ*, **330**, 104-105.

McClelland,DBL. & Contreras,M. (2005b) Effectiveness and safety of blood transfusion: have we lost the plot? *Journal of Royal College of Physicians Edinburgh*, **35**, 2-4.

McClelland,DBL. (2007) *Handbook of Transfusion Medicine*, 4th Edition. Norwich, The Stationery Office.

McClelland,DBL. (personal communication) Strategy Director, Scottish National Blood Transfusion Service, Edinburgh.

McGill,N., O'Shaughnessy,D., Pickering,R., Herbertson,M., & Gill,R. (2002) Mechanical methods of reducing blood transfusion in cardiac surgery: randomised controlled trial. *British Medical Journal*, **324**, 1299.

Medicines and Healthcare Products Regulatory Agency (MHRA) (online) *http://www.mhra.gov.uk*

Moss, L. (2007) Fears for blood supplies as CJD test set to cut flow of potential donors. *The Scotsman* 09/08/2007.

Murphy,M. (2005) Strategies for reducing the exposure to donor blood. *Clinical Medicine*, **5**, 337-340.

National Institute for Health and Clinical Excellence (NICE). (2006) Patient safety and reduction of risk of transmission of Creutzfeldt-Jakob disease (CJD) via interventional procedures. IPG196. National Institute for Health and Clinical Excellence, NHS.

Nightingale,S., Wanamaker,V., Silverman,B., McCurdy,P., McMurtry,L., Quarles,P., Sandler,SG., Triulzi,D., Whitsett,C., Hillyer,C., McCarthy,L., Goldfinger,D., & Satcher,D. (2003) Use of sentinel sites for daily monitoring of the US blood supply. *Transfusion*, **43**, 364-372.

O'Reilly,O. (2004) National Blood Strategy Implementation Group: Report to the Minister for Health and Children. Part 4: Blood utilisation survey for year 2001. Irish Blood Transfusion Service.

Palmer , J (personal communication) Effective Use of Blood Group, Scottish National Blood Transfusion Service

Palermo,G., Bove,J., & Katz,AJ. (1980) Patterns of blood use in Connecticut. *Transfusion*, **20**, 704-710.

Palo,R., Capraro,L., Hovilehto,S., Koivuranta,M., Krusius,T., Loponen,E., Mantykoski,R., Pentti,J., Pitkanen,O., Raitakari,M., Rimpilainen,J., Salmenpera,M., Salo,H., & Maki,T. (2006a) Population-based audit of fresh-frozen plasma transfusion practices. *Transfusion*, **46**, 1921-1925.

Palo,R., Ali-Melkkila,T., Hanhela,R., Jantti,V., Krusius,T., Leppanen,E., Mahlamaki,E.K., Perhoniemi,V., Rajamaki,A., Rautonen,J., Salmenpera,M., Salo,H., Salonen,I., Savolainen,E.R., Sjovall,S., Suistomaa,M., Syrjala,M., Tienhaara,A., Vahamurto,M., & Maki,T. (2006b) Development of permanent national register of blood component use utilizing electronic hospital information systems. *Vox Sanguinis*, **91**, 140-147.

Pareira,A. (2004) Performance of time-series methods in forecasting the demand for red blood cell transfusion. *Transfusion Practice*, **44**, 739-746.

Pinkerton,PH., Seigel,C., & Coovadia,AS. (1993) Transfusion practice in support of seven common surgical procedures. *Canadian Society for Transfusion Medicine (CSTM) Bulletin*, **5**(2), 26-32.

Pinkerton,PH. (2002) Norman Bethune and transfusion in the Spanish Civil War. *Vox Sanguinis*, **83**, 117-120.

Pisoni,R. & Remuzzi,G. (2000) Thrombotic microangiopathy. *European Journal of Internal Medicine*, **11**, 135-139.

Pitocco,C. & Sexton,TR. (2005) Alleviating blood shortages in a resource-constrained environment. *Transfusion*, **45**, 1118-1126.

Provan,D. (1999) Better Blood Transfusion. *BMJ*, **318**, 1435-1436.

Regan,F. (2004) New donors, new recipients--who gets what in 2003? *Transfusion Clinique et Biologique*, **11**, 53-56.

Savoia,HF., Metz,J., Maxwell,EL., Hauesler,MN., Mellor,J., & Kiely,S. (2002) Utilization of pre-operative autologous blood donation in elective surgery. *ANZ Journal of Surgery*, **72**, 557-560.

Schreiber,GB., Glynn,SA., Busch,MP., Sharma,UK., Wright,DJ., & Kleinman,SH. (2001) Incidence rates of viral infections among repeat donors:are frequent donors safer? *Transfusion*, **41**, 730-735.

Scottish Arthroplasty Project. (2007) Scottish Arthorplasty Project Annual 2007. NHS Scotland.

Scottish Executive Health Department. (1999a) Better Blood Transfusion. NHS MEL(1999)9. Scottish Executive Health Department, Scottish Executive.

Scottish Executive Health Department. (1999b) Variant Creutzelt-Jakob Disease (vCJD): minimising the risk of transmission. NHS MEL (1999)65. Scottish Executive Health Department, Scottish Executive.

Scottish Executive Health Department and Directorate of Service Policy and Planning. (2003) NHS HDL(2003)19. Scottish Executive Health Department, Scottish Executive.

Scottish Intercollegiate Guidelines Network (SIGN). (2001) SIGN Guidelines No.54: Peri-operative blood transfusion for elective surgery. 1-899893-77-6. Edinburgh, Scottish Intercollegiate Guidelines Network. *http://www.sign.ac.uk/guidelines/fulltext/54/index.html.*

Scottish National Blood Transfusion Service (SNBTS) (online) "Who can give blood?" website guidelines. http://*www.scotblood.co.uk/who_can_donate.html*

Shehata,N., Naglie,G., Alghamdi,AA., Callum,J., Mazer,CD., Hebert,P., Streiner,D., & Wilson,K. (2007) Risk factors for red cell transfusion in adults undergoing coronary artery bypass surgery: a systematic review. *Vox Sanguinis*, **93**, 1-11.

Sirchia,G., Giovanetti,AM., McClelland,DBL., & Fracchia,GN. (1994) Safe and good use of blood in surgery (SANGUIS). Luxembourg, Biomedical and Health Research, European Commission on Medicine and Health.

Smith,R. (2005) Doctors question whether all blood transfusions are effective and necessary. *British Medical Journal*, **330**, 558.

Spencer,J., Thomas,S., Yardy,G., Mukudan,C., & Barrington,R. (2005) Are we overusing blood transfusion after elective joint replacement? A simple method to reduce the use of a scarce resource. *Annals of The Royal College of Surgeons of England*, **87**(3), 28-30.

Stack, E (personal communication) Scottish National Blood Transfusion Service, Edinburgh

Stanworth,SJ., Cockburn,H., Boralessa,H., & Contreras,M. (2002) Which groups of patients are transfused? A study of red cell usage in London and southeast England. *Vox Sanguinis*, **83**, 352-357.

Stanworth,SJ., Brunskill,SJ., Hyde,CJ., McClelland,DBL., & Murphy,MF. (2004) Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. *British Journal of Haematology*, **126**, 139-152.

Stewart, A (personal communication) Blood Use Data Project Manager, Better Blood Transfusion Programme, Edinburgh.

Sullivan,MT., McCullough,J., Schreiber,GB., & Wallace,EL. (2002) Blood collection and transfusion in the United States in 1997. *Transfusion*, **42**, 1253-1260.

Sullivan,MT. & Wallace,EL. (2005) Blood collection and transfusion in the United States in 1999. *Transfusion*, **45**, 141-148.

Sullivan,MT., Cotten,R., Read,EJ., & Wallace,EL. (2007) Blood collection and transfusion in the United States in 2001. *Transfusion*, **47**, 385-394.

Surgenor,D., Wallace,E., Churchill,W., Hao,S., Hale,W., & Schnitzer,J. (1989) Utility of DRG and ICD-9-CM classification codes for the study of transfusion issues. Transfusions in patients with digestive diseases. *Transfusion*, **29**, 761-767.

Surgenor,D., Wallace,E., Hale,S., & Gilpatrick,M. (1998) Changing patterns of blood transfusion in four sets of United States hospitals, 1980 to 1985. *Transfusion*, **28**, 513-518.

Surgenor,DM., Wallace,EL., Churchill,WH., Hao,SH., Chapman,RH., & Poss,R. (1991) Red cell transfusions in total knee and total hip replacement surgery. *Transfusion*, **31**, 531-537.

Surgenor,DM., Wallace,EL., Churchill,WH., Hao,SH., Chapman,RH., & Collins,JJ. (1992) Red cell transfusions in coronary artery bypass surgery (DRGs 106 and 107). *Transfusion*, **32**, 458-464.

Surgenor,DM., Churchill,WH., Wallace,EL., Rizzo,RJ., Chapman,RH., McGurk,S., Bertholf,MF., Goodnough,LT., Kao,KJ., Koerner,TA., Olson,JD., & Woodson,RD. (1996) Determinants of red cell, platelet, plasma, and cryoprecipitate transfusions during coronary artery bypass graft surgery: the Collaborative Hospital Transfusion Study. *Transfusion*, **36**, 521-532.

Syrjäla,MT., Kytoniemi,I., Mikkolainen,K., Ranimo,J., & Lauharanta,J. (2001) Transfusion practice in Helsinki University Central Hospital: an analysis of diagnosis-related groups (DRG). *Transfusion Medicine*, **11**, 423-431.

Taylor,C. (2005) Chapter 16: Transfusion triggers in medical patients with chronic anaemia. In: *A manual for blood conservation.* Editors: Thomas,D., Thompson,J., & Ridler,B., Shrewsbury, tfm Publishing Ltd..

The Safe and Good Use of Blood in Surgery (SANGUIS) Study Group. (1994) Use of blood products for elective surgery in 43 European hospitals. *Transfusion Medicine,* **4,** 251-268.

Thomas,M. (2005) Chapter 1: Blood letting and blood giving - A history of blood transfusion. In: *A manual for blood conservation.* Editors: Thomas,D., Thompson,J., & Ridler,B., Shrewsbury, tfm Publishing Ltd..

Thomson,RA., Bethel,J., Lo,AY., Ownby,HE., Nass,CC., & Williams,AE. (1998) Retention of "safe" blood donors. The Retrovirus Epidemiology Donor Study. *Transfusion,* **38,** 359-367.

Tinmouth,A., Macdougall,L., Fergusson,D., Amin,M., Graham,ID., Hebert,PC., & Wilson,K. (2005) Reducing the amount of blood transfused: a systematic review of behavioural interventions to change physicians' transfusion practices. *Archives of Internal Medicine,* **165,** 845-852.

Titlestad,K., Georgsen,J., Jorgensen,J., & Kristensen,T. (2001) Monitoring transfusion practices at two university hospitals. *Vox Sanguinis,* **80,** 40-47.

Titlestad,K., Kristensen,T., Jorgensen,J., & Georgsen,J. (2002) Monitoring transfusion practice - a computerized procedure. *Transfusion Medicine,* **12,** 25-34.

Torella,F., Haynes,SL., Bennett,J., Sewell,D., & McCollum,CN. (2002) Can hospital transfusion committees change transfusion practice? *Journal of the Royal Society of Medicine,* **95,** 450-452.

Tynell,E., Norda,R., Montgomery,SM., & Bjorkman,A. (2005) Diagnosis and procedure-specific survival among transfusion of recipients in 1993 and 2000, Orebro County, Sweden. *Vox Sanguinis,* **88,** 181-188.

UK Blood Transfusion Services (UKBTS) (online) Better Blood Transfusion Toolkit. *www.transfusionguidelines.org.uk/index.asp?Publication=BBT&Section=22&pageid=476*

Vamvakas,EC. & Taswell,HF. (1994) Epidemiology of blood transfusion. *Transfusion,* **34,** 464-470.

Wallace,EL., Surgenor,DM., Hao,HS., An,J., Chapman,RH., & Churchill,WH. (1993) Collection and transfusion of blood and blood components in the United States, 1989. *Transfusion,* **33,** 139-144.

Wallace,EL., Churchill,WH., Surgenor,DM., Cho,GS., & McGurk,S. (1998) Collection and transfusion of blood and blood components in the United States, 1994. *Transfusion,* **38,** 625-636.

Wallace,EL. (2003) Monitoring the nation's blood supply. *Transfusion,* **43,** 299-301.

Wallis,JP., Stainsby,D., & McClelland,DBL. (2002) Audit of red cell transfusion. *Transfusion Medicine*, **12**, 1-9.

Wallis,JP., Wells,AW., Matthews,JN., & Chapman,CE. (2004) Long-term survival after blood transfusion: a population based study in the North of England. *Transfusion*, **44**, 1025-1032.

Wallis,JP., Wells,AW., & Chapman,CE. (2006) Changing indications for red cell transfusion from 2000 to 2004 in the North of England. *Transfusion Medicine*, **16**, 411-417.

Walsh,TS., McArdle,F., Chohan,S., McEntergart,M., Fisher,A., & McClelland,DBL. (2001) Red cell transfusion in critically ill patients: Audit of current practice in the Royal Infirmary of Edinburgh ICU (Ward 15). Unpublished.

Walsh,TS. & McClelland,DBL. (2003) When should we transfuse critically ill and peri-operative patients with known coronary artery disease?. *British Journal of Anaesthesia*, **90**, 719-722.

Walsh,TS., Garrioch,M., Maciver,C., Lee,RJ., MacKirdy,F., McClelland,D., Kinsella,J., & Wallis,C. (2004) Red cell requirements for intensive care units adhering to evidence-based transfusion guidelines. *Transfusion*, **44**, 1405-1411.

Wells,AW., Mounter,PJ., Chapman,CE., Stainsby,D., & Wallis,JP. (2002) Where does blood go? Prospective observational study of red cell transfusion in north England. *BMJ*, **325**, 803.

Wells,AW. (2004) Who uses blood? *Vox Sanguinis*, **87**, 146-148.

Williamson, L. (2003) Epidemiology and survival of transfusion recipients (EASTR): Grant Protocol. Unpublished.

World Health Organisation Media Centre. (2002) Fact sheet 180: Variant Creutzfeldt-Jakob Disease. *http://www.who.int/mediacentre/factsheets/fs180/en.* World Health Organisation, online.

World Health Organisation (WHO). (2004) Global Database on Blood Safety Report 2001-2002. *http://www.who.int/bloodsafety/global_database/en.* World Health Organisation, online.

Zimmermann,R., Buscher,M., Linhardt,C., Handtrack,D., Zingsem,J., Weisbach,V., & Eckstein,R. (1997) A survey of blood component use in a German university hospital. *Transfusion*, **37**, 1075-1083.

Zimmermann,R., Handtrack,D., Zingsem,J., Weisbach,V., Neidhardt,B., Glaser,A., & Eckstein,R. (1998) A survey of blood utilization in children and adolescents in a German university hospital. *Transfusion Medicine*, **8**, 185-194.